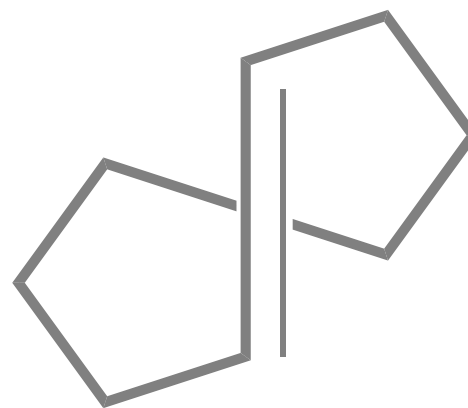


Strained-Olefin Catalysts Open The New Horizon of Chemistry

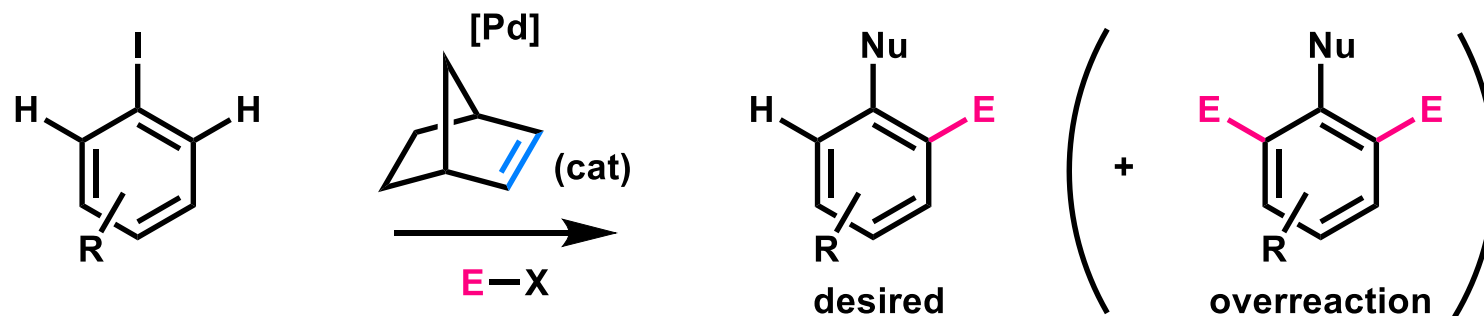


2018.10.27
Haruka Fujino

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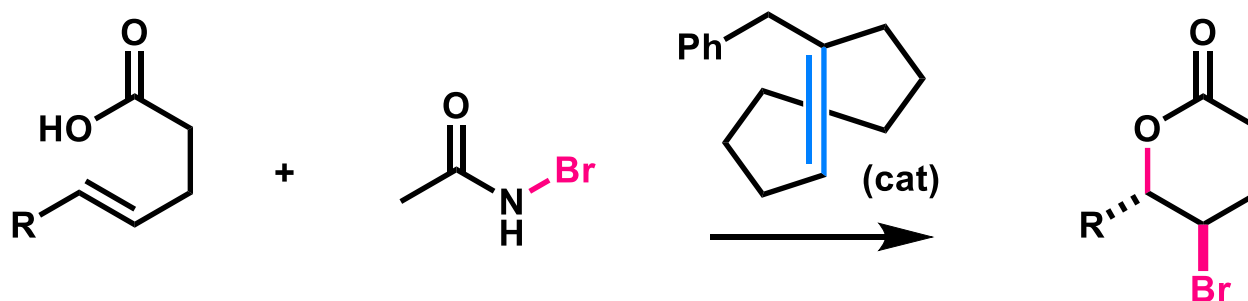
1. Introduction

2. Norbornene-Derived Catalysts; Improvement of Catellani Reaction (Guanbin Dong, 2018)



3. *Trans*-Olefin catalysts

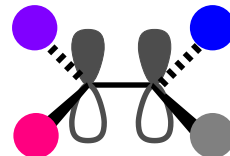
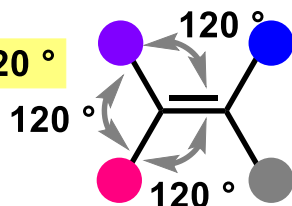
Trans-Cyclooctenes as Halolactonization Catalyst (Matsubara, 2018)



Examples of Strained Olefins¹⁾

normal olefin

1) bond angles = 120°



2) 6 atoms on the same π plane

1) bond angles $\neq 120^\circ$



2) 6 atoms NOT on the same π plane

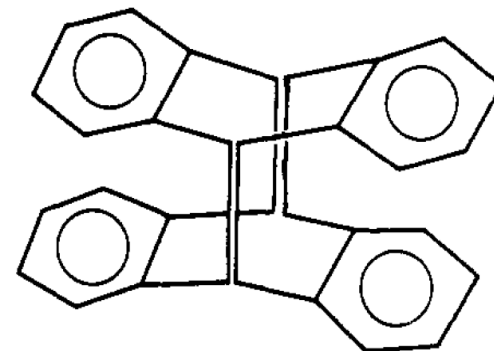
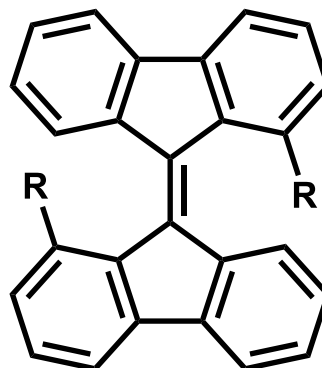
small ring



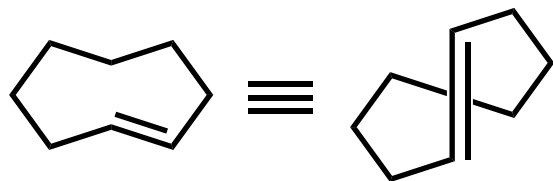
bridged cyclic



rotationally distorted

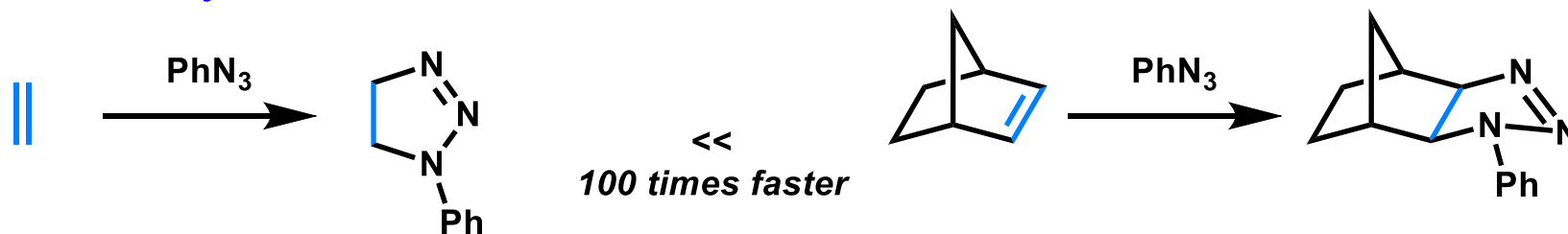


trans-olefin

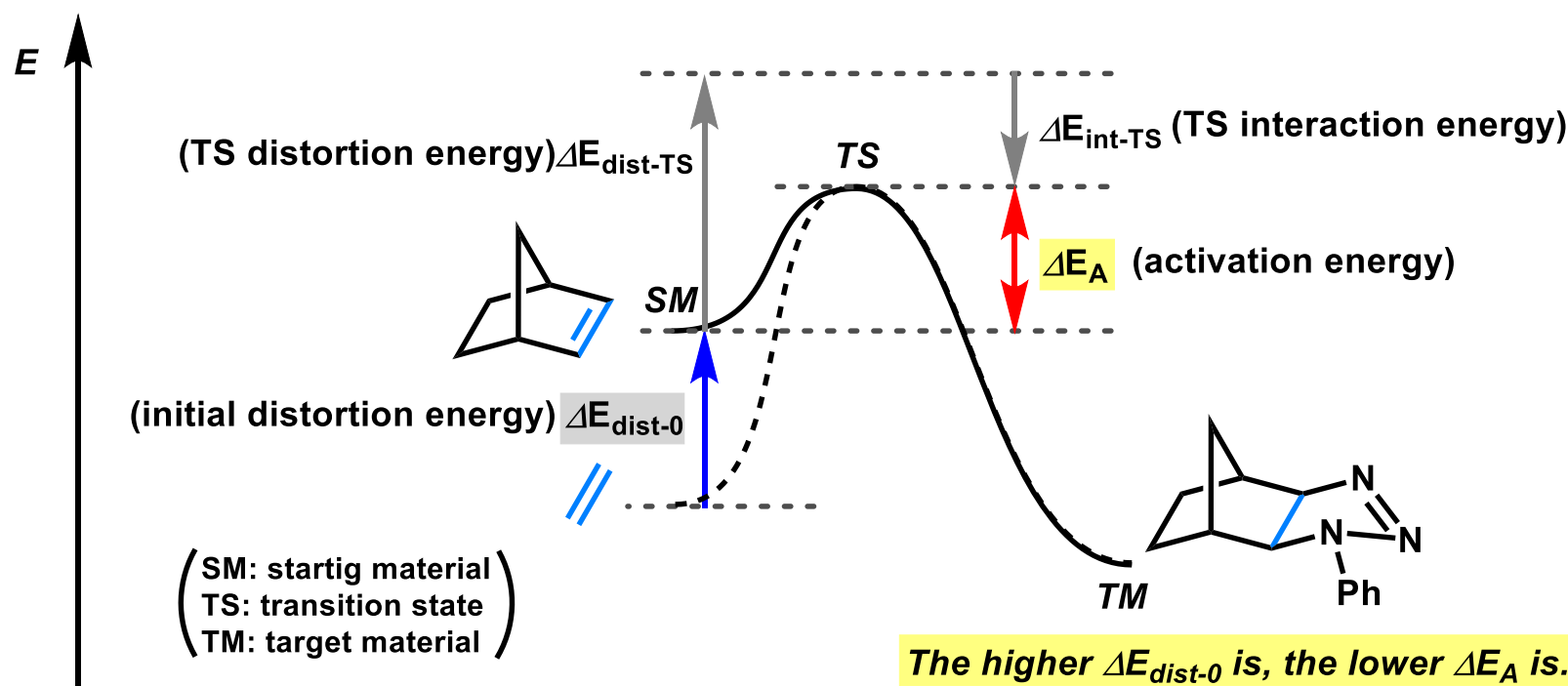


High Reactivity of Strained Olefins

initial discovery¹⁾



distortion-interaction model²⁾

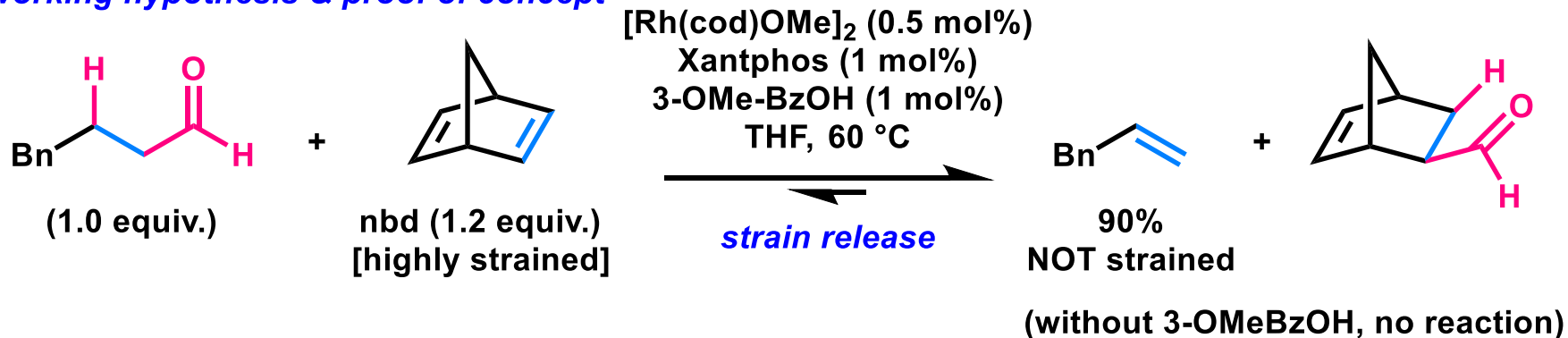


1) Alder, K.; Stein, G. *Liebigs Ann. Chem.* **1931**, 485, 211.

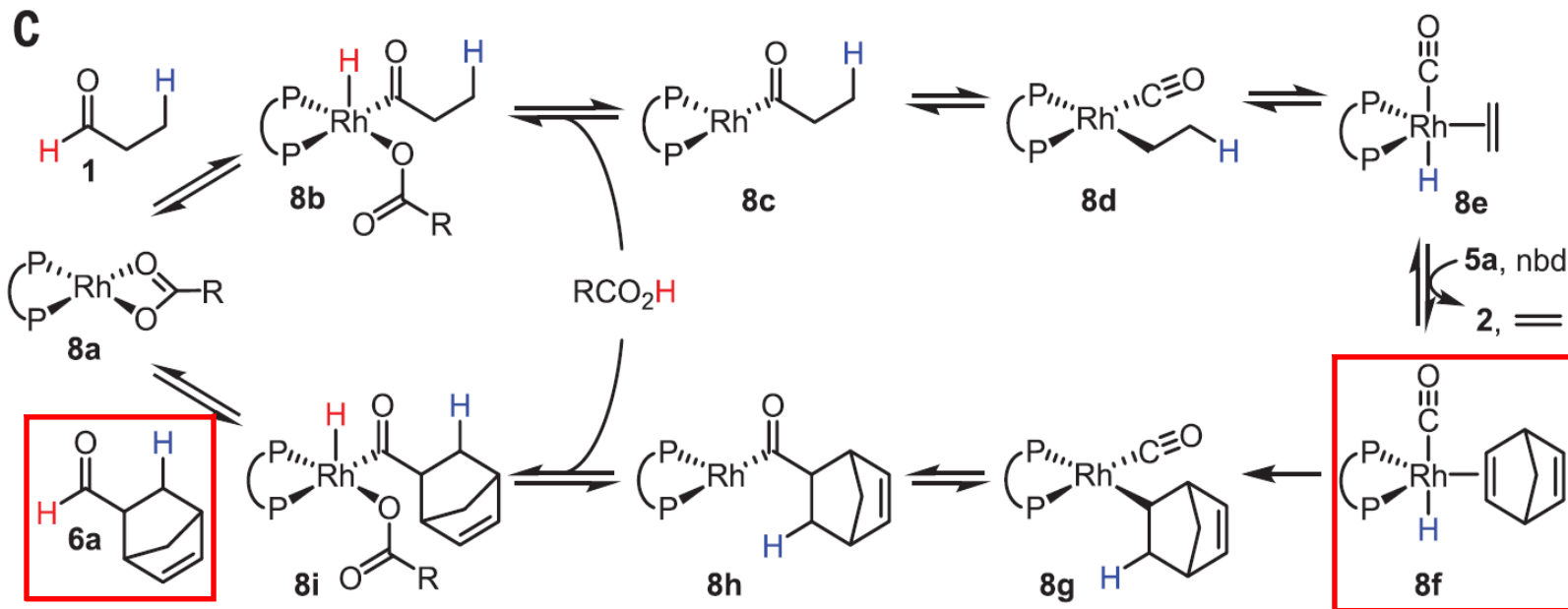
2) Schoenebeck, F.; Ess, D. H.; Jones, D. O.; Houk, K. N. *J. Am. Chem. Soc.* **2009**, 131, 8121.

Control of Equilibrium; Transfer Hydroformylation¹⁾

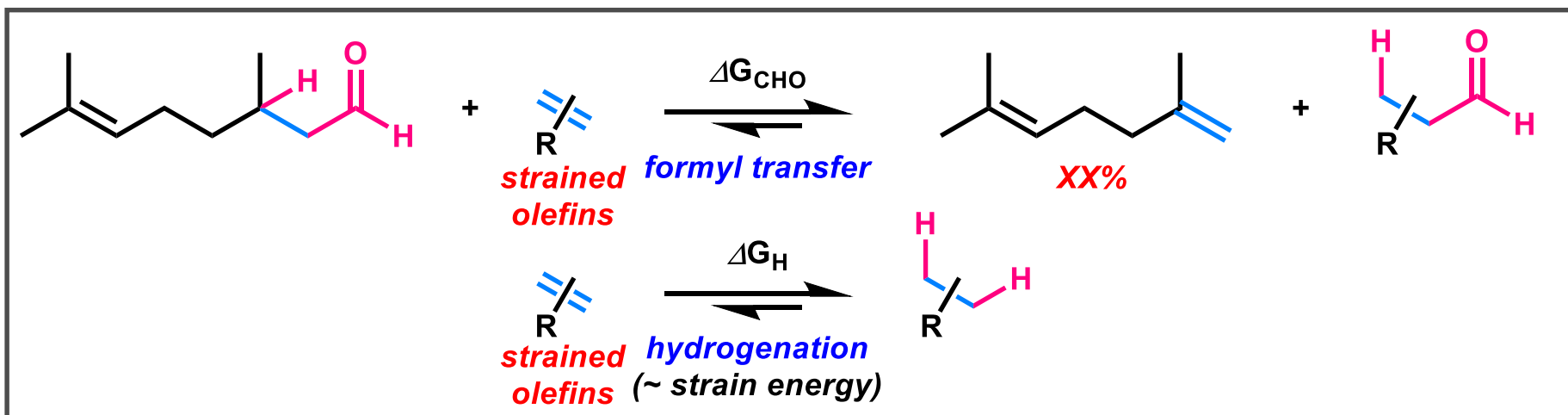
working hypothesis & proof of concept



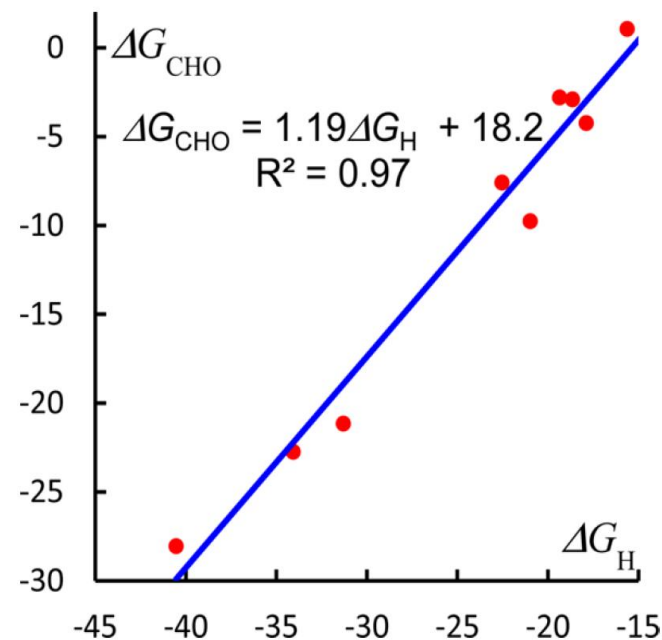
reaction mechanism



Prediction of Formyl Acceptors by DFT Calculation¹⁾



<i>strained olefins</i>	ΔG_{CHO}^a (kcal/mol)	ΔG_{H}^a (kcal/mol)	experimental ²⁾ yields (XX%)
(nbe)			
	-2.9	-18.6	97% (at 40 °C)
(bnbd)			
	-7.6	-22.5	99% (at 22 °C)
(n = 1)	-28.1	-40.5	no data
(n = 2)	-4.2	-17.9	no data
(n = 4)	1.1	-15.6	no data
R——H			
(R = H)	-22.7	-34.1	no data
(R = Ph)	-21.1	-31.3	no data



^a (Gaussian 09/M11-L/6-31G(d))

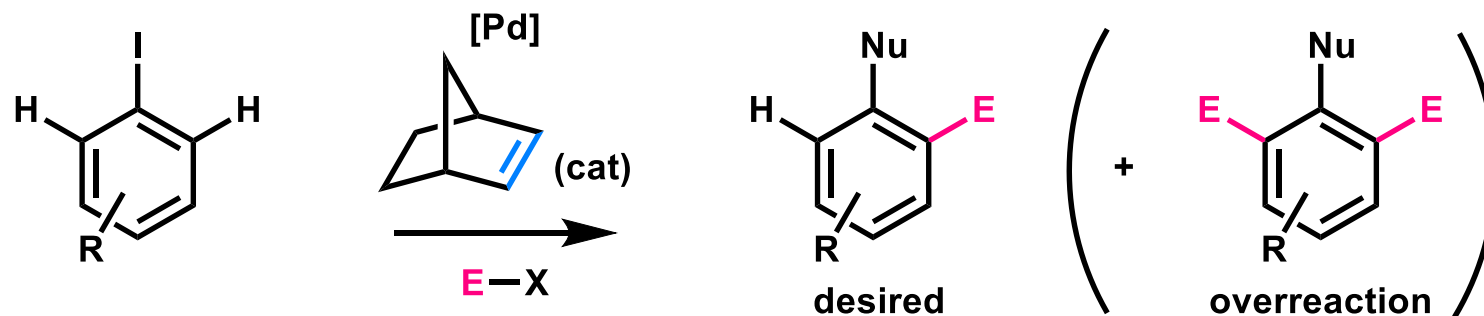
1) Chen, C. and Lan, Y. *J. Org. Chem.* **2016**, 81, 2320.

2) Murphy, S. K.; Park, J.-W.; Cruz, F. A.; Dong, V. M. *Science* **2015**, 347, 56.

Contents

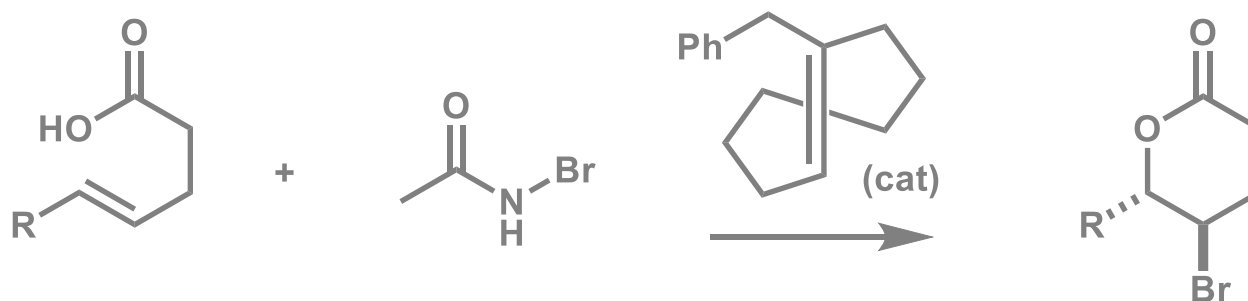
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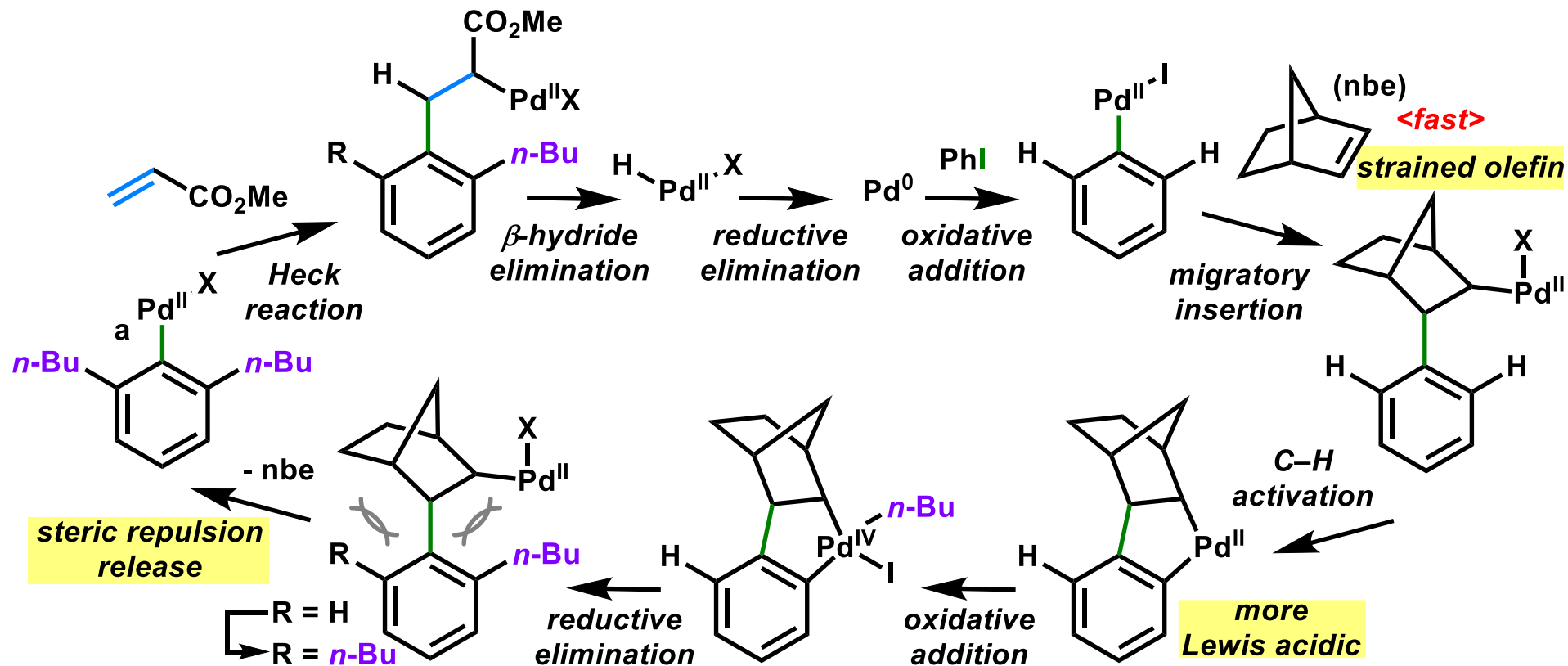
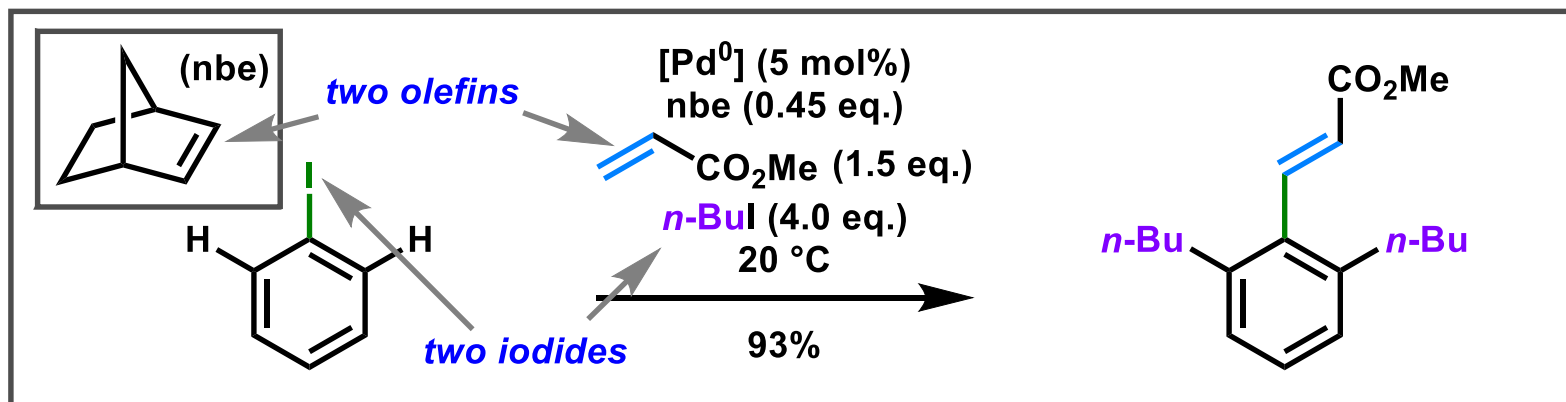


3. *Trans*-Olefin catalysts

Trans-Cyclooctenes as Halolactonization Catalyst (Matsubara, 2018)



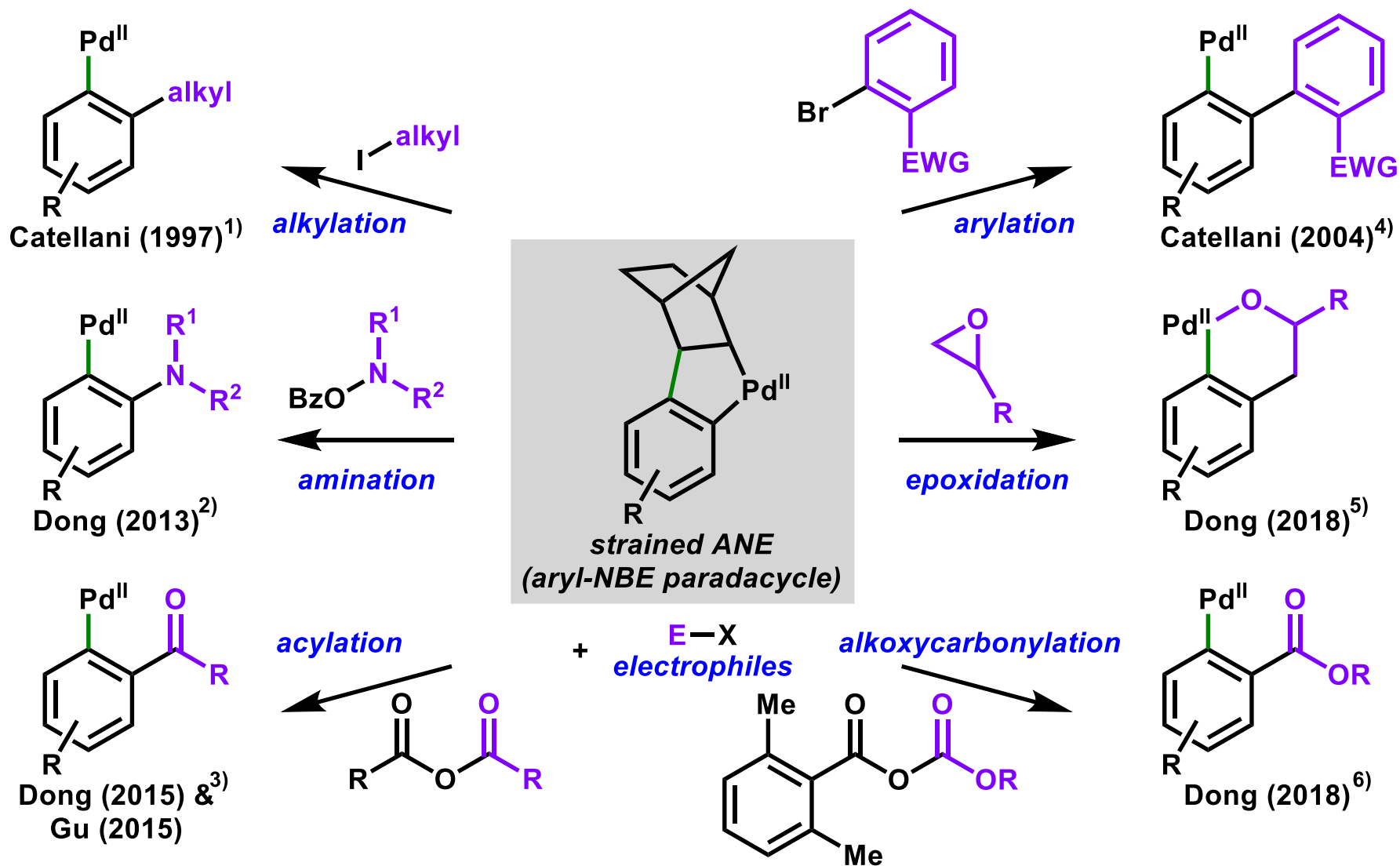
Catellani Reaction¹⁾



1) Catellani, M.; Frignani, F.; Rangoni, A. *Angew. Chem. Int. Ed.* **1997**, 36, 119.

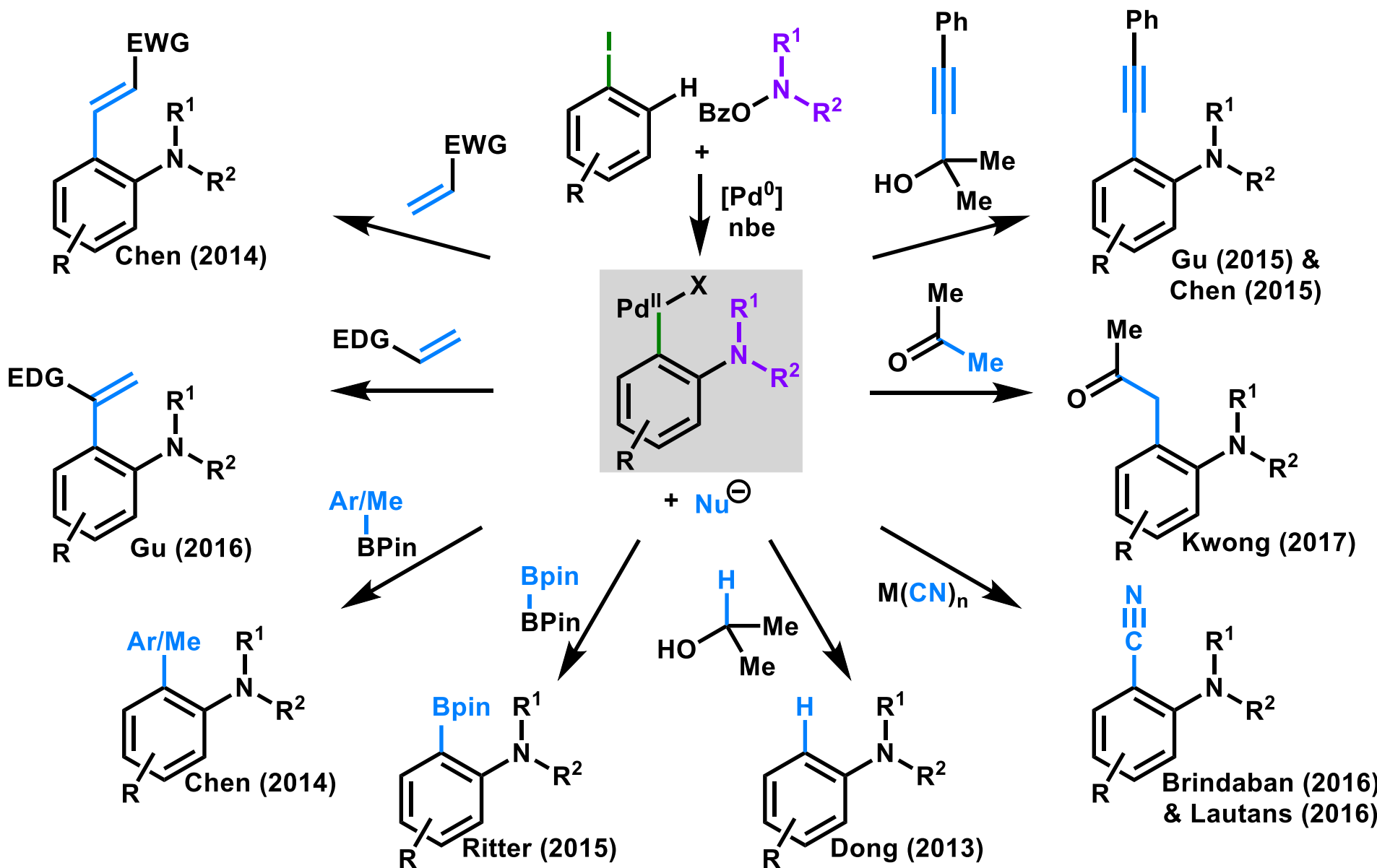
2) For a related LS on Catellani reaction, see; 121112_LS_Shunichiroh_Katoh.

Recent Advances (1): Electrophiles Expansion



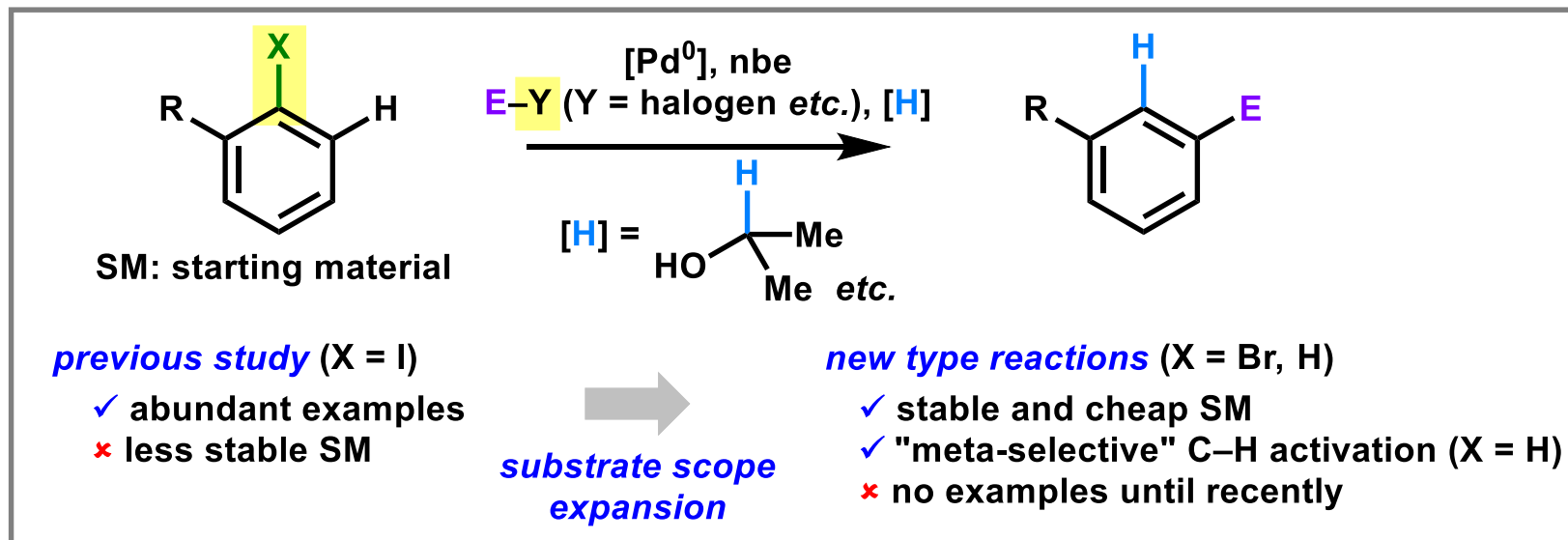
1) Catellani, M. et al. *Angew. Chem. Int. Ed.* **1997**, 36, 119. 2) Dong, G. et al. *J. Am. Chem. Soc.* **2013**, 135, 18350. 3) (a) Dong, G. et al. *Angew. Chem. Int. Ed.* **2015**, 54, 12664. (b) Gu, Z. H. et al. *Angew. Chem. Int. Ed.* **2015**, 54, 12669. 4) Catellani, M. et al. *J. Am. Chem. Soc.* **2004**, 126, 78. 5) Dong, G. et al. *Org. Chem. Front.* **2018**, doi: 10.1039/C8QO00808F. 6) Dong, G. et al. *Chem* **2018**, 1, 581.

Recent Advances (2): Nucleophiles Expansion¹⁾

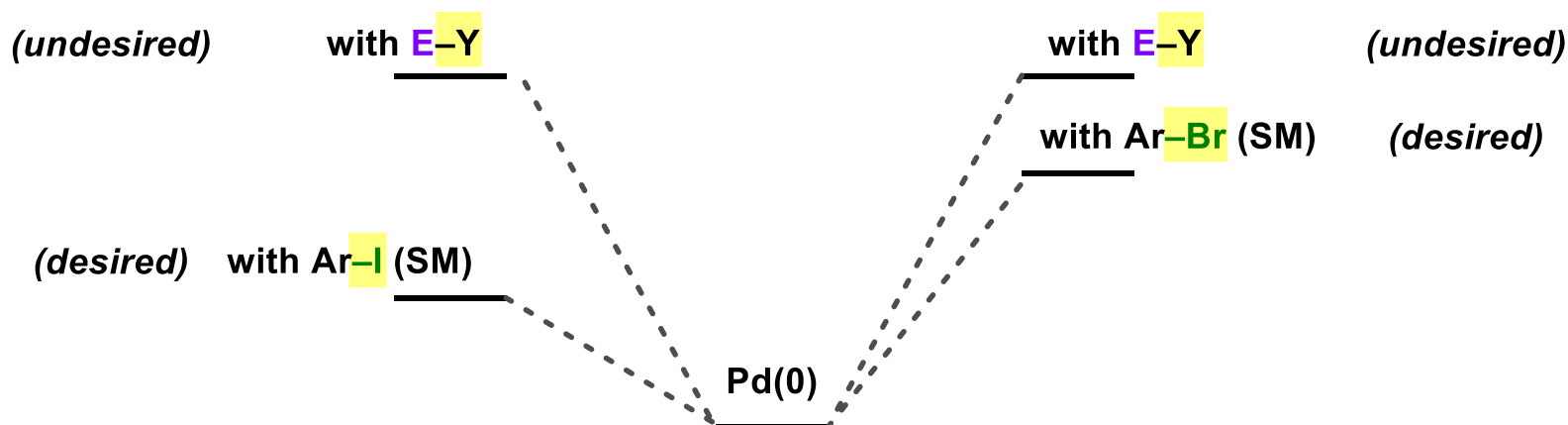


1) Dong, G. *et al.* *J. Am. Chem. Soc.* **2018**, *140*, 8551. and references herein.

Recent Advances (3): Starting Material Expansion-1

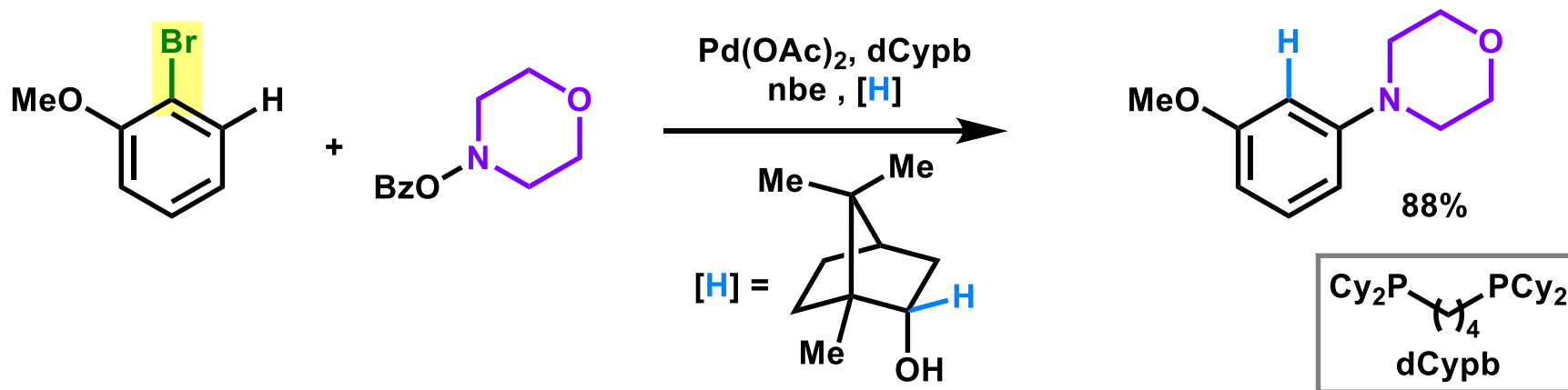


required selectivity (X = I, Br)

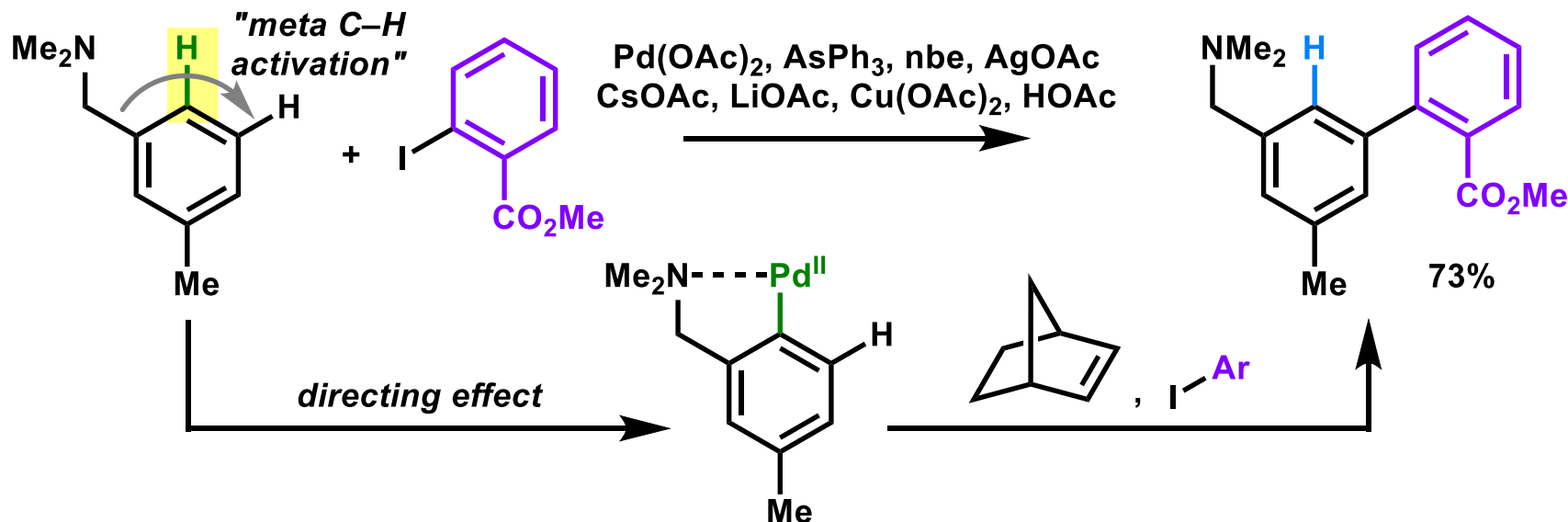


Recent Advances (3): Start Materials Expansion-2

ortho amination of bromo arene¹⁾



meta C-H amination²⁾

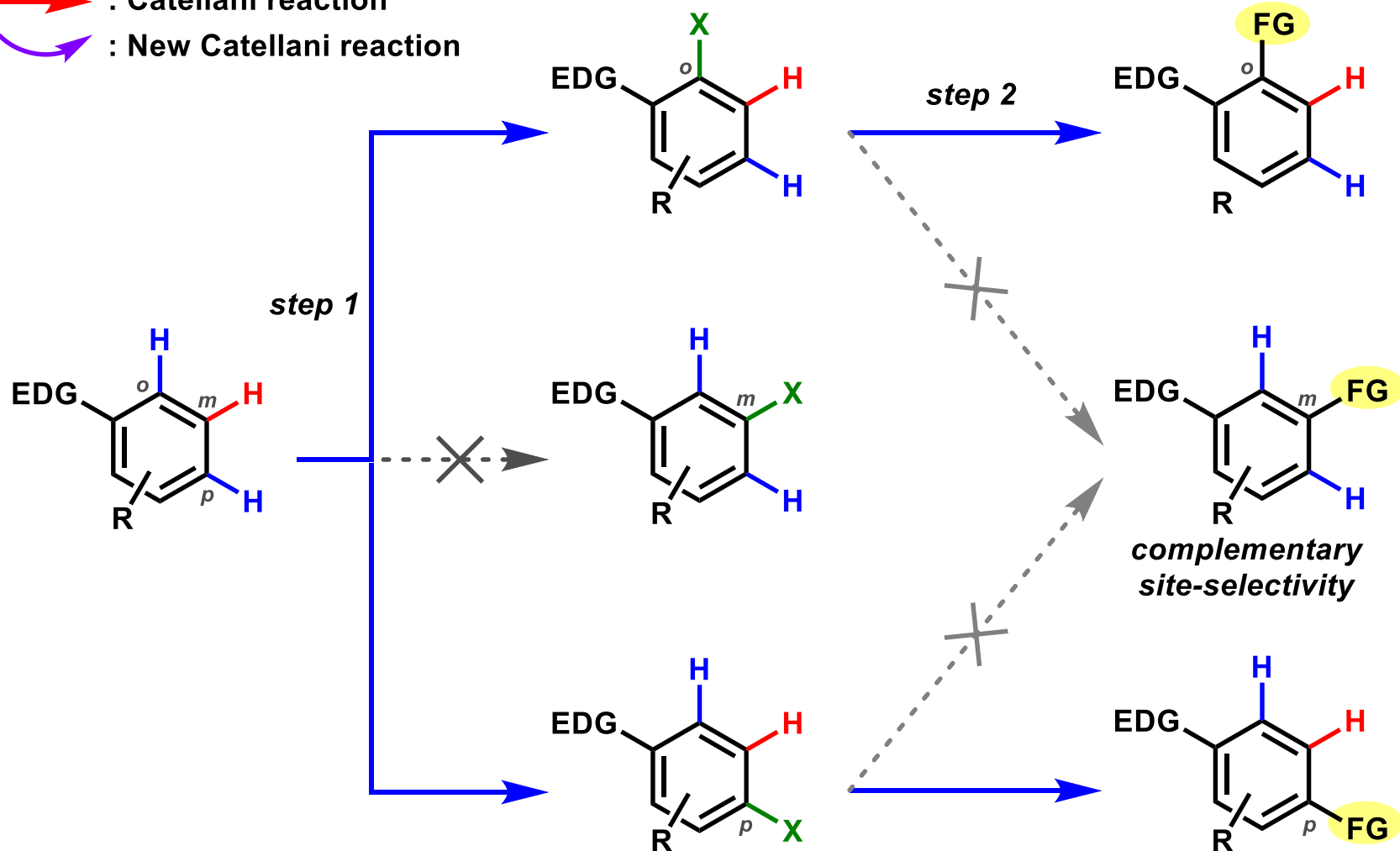


1) Dong, Z.; Lu, G.; Wang, J.; Liu, P.; Dong, G. *J. Am. Chem. Soc.* **2018**, *140*, 8551.

2) Dong, Z.; Wang, J.; Dong, G. *J. Am. Chem. Soc.* **2015**, *137*, 5887.

Advantageous Points of Catellani Reaction

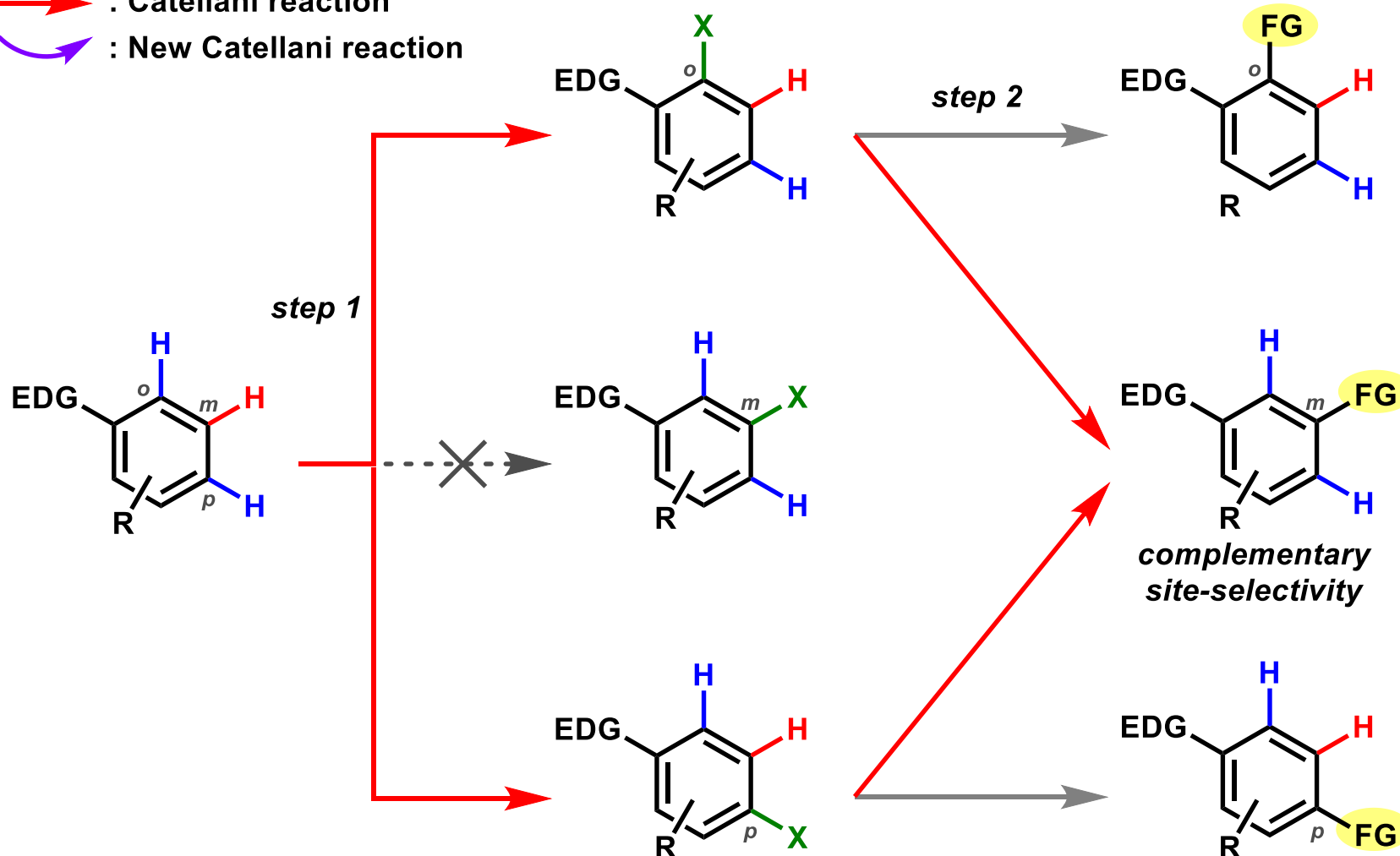
- : conventional strategy
- : Catellani reaction
- : New Catellani reaction



In case of EWG, not EDG, the similar "complementary site-selectivity" can be observed.

Advantageous Points of Catellani Reaction

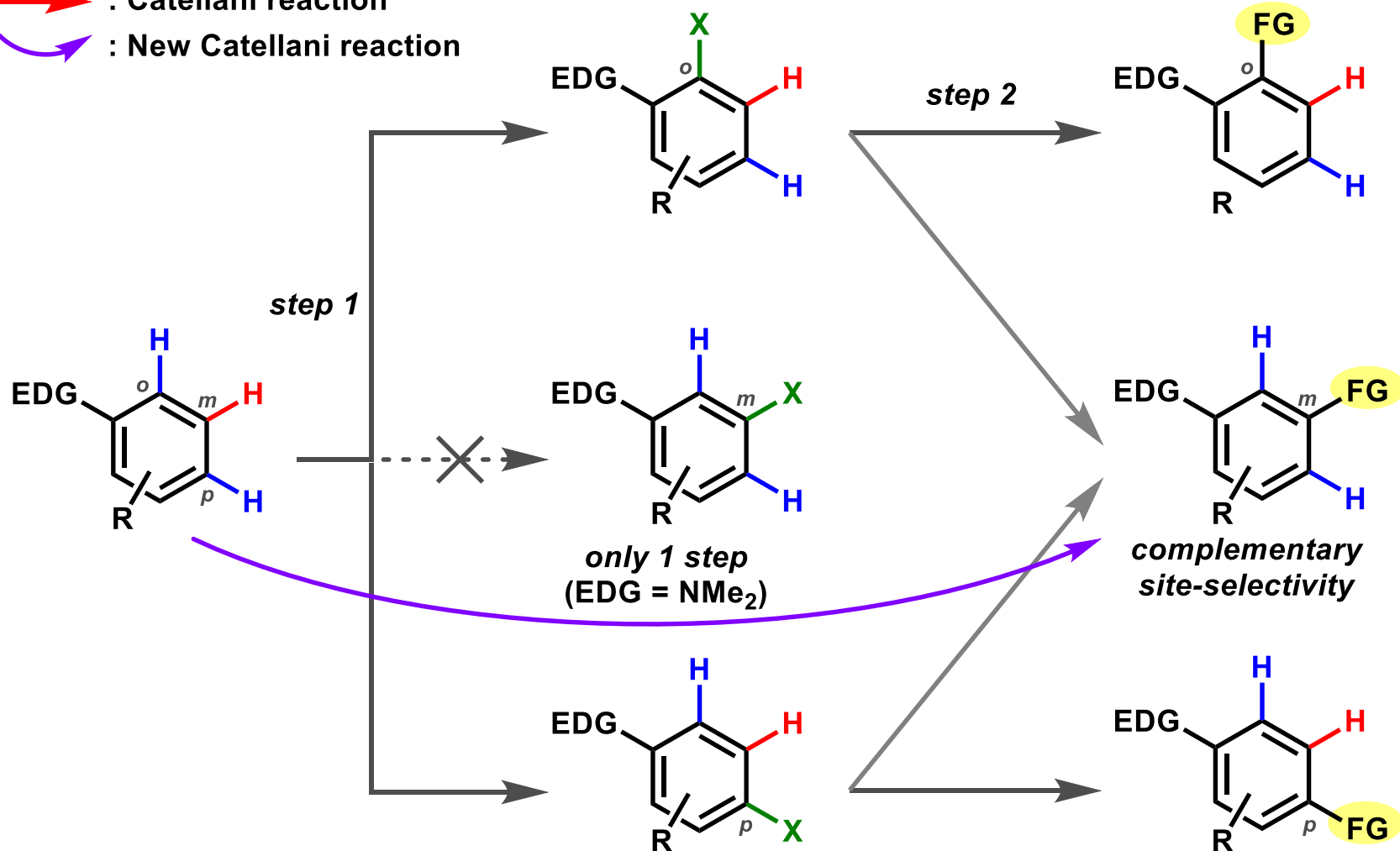
- : conventional strategy
- : Catellani reaction
- : New Catellani reaction



In case of EWG, not EDG, the similar "complementary site-selectivity" can be observed.

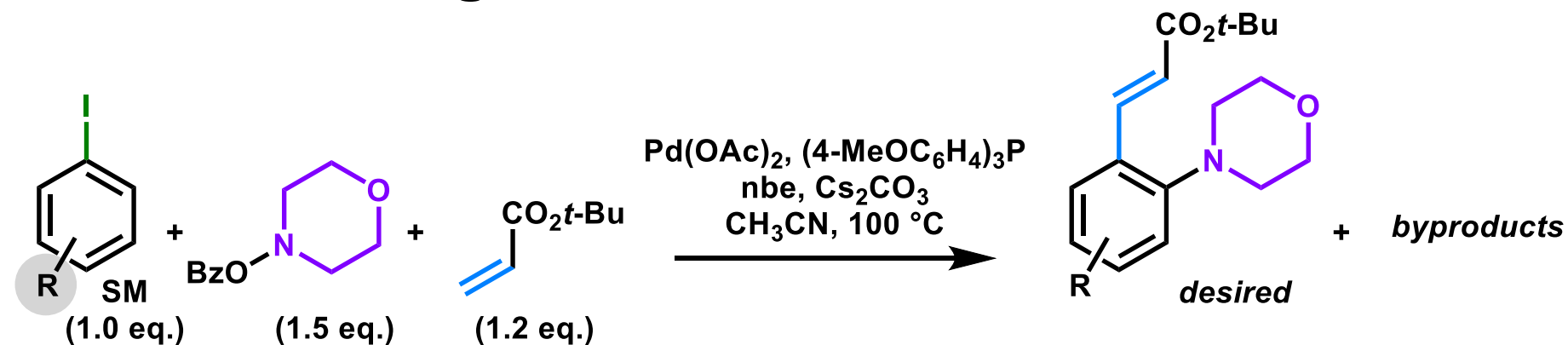
Advantageous Points of Catellani Reaction

- : conventional strategy
- : Catellani reaction
- : New Catellani reaction

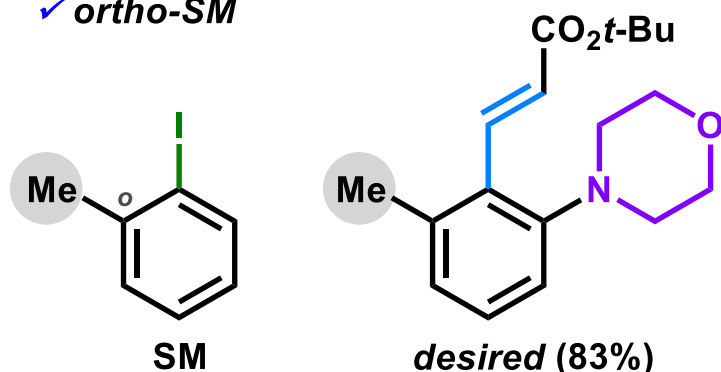


In case of EWG, not EDG, the similar "complementary site-selectivity" can be observed.

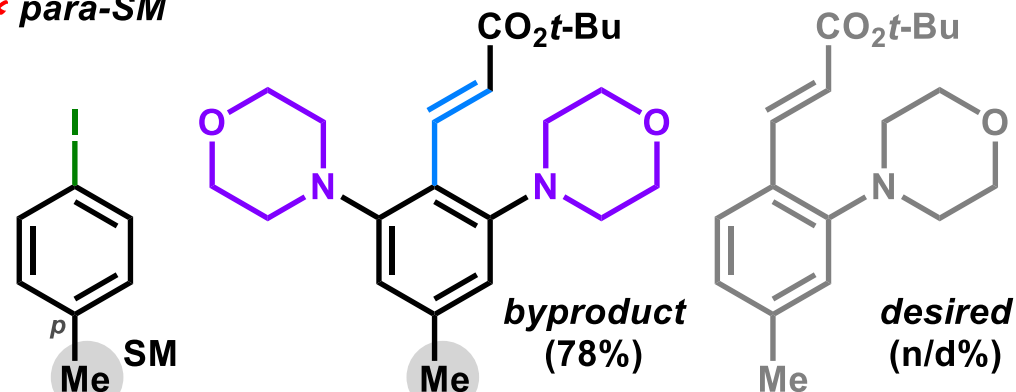
Remaining Problems: *Ortho*-Constraint¹⁾



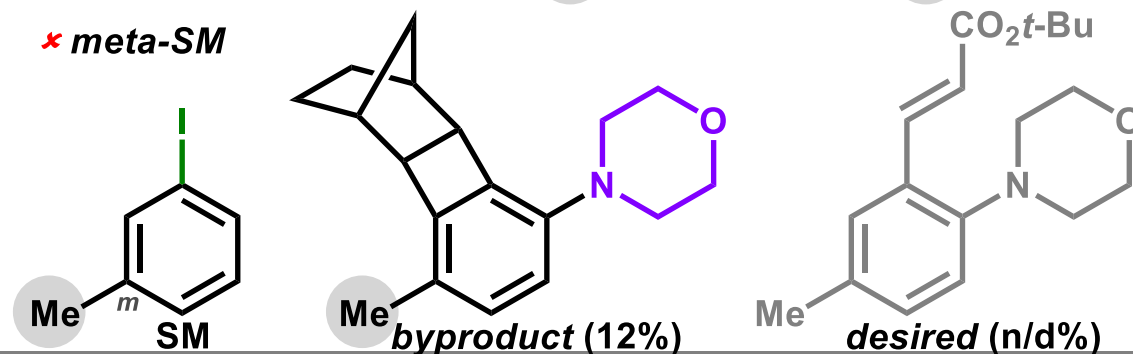
✓ *ortho*-SM



✗ *para*-SM



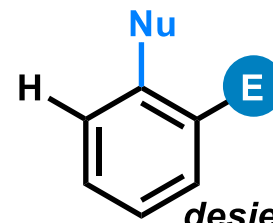
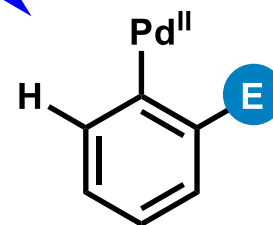
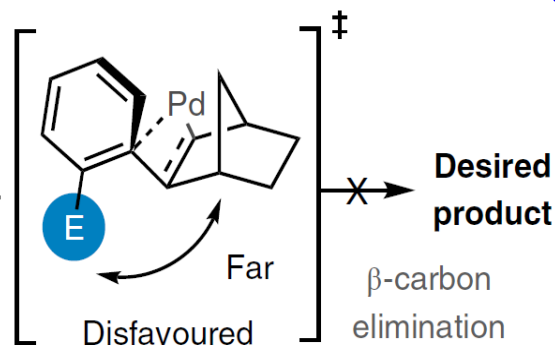
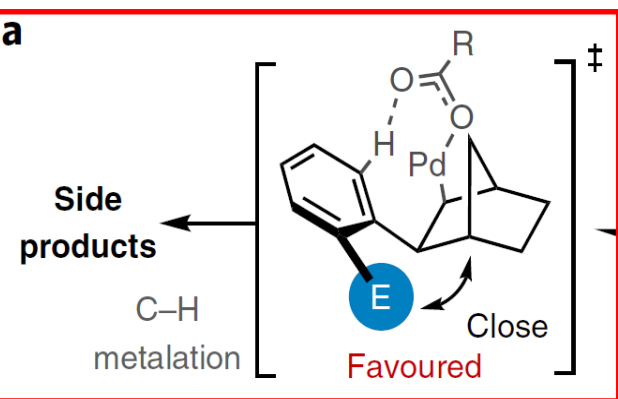
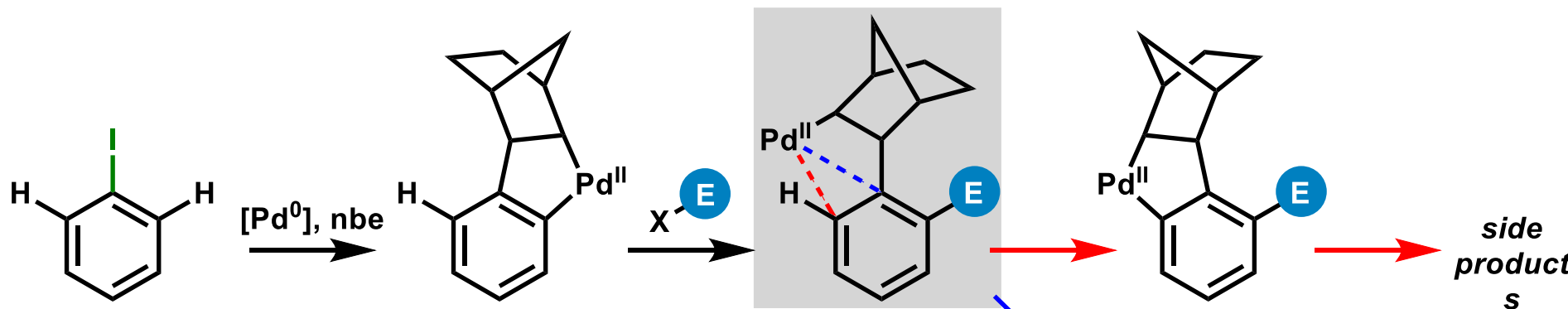
✗ *meta*-SM



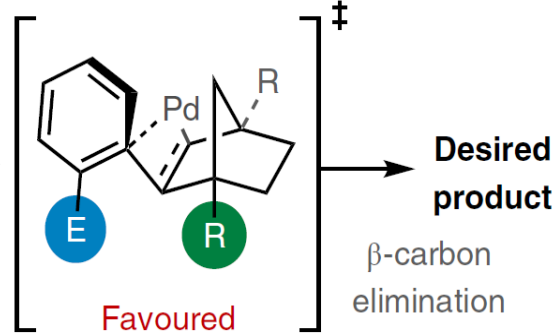
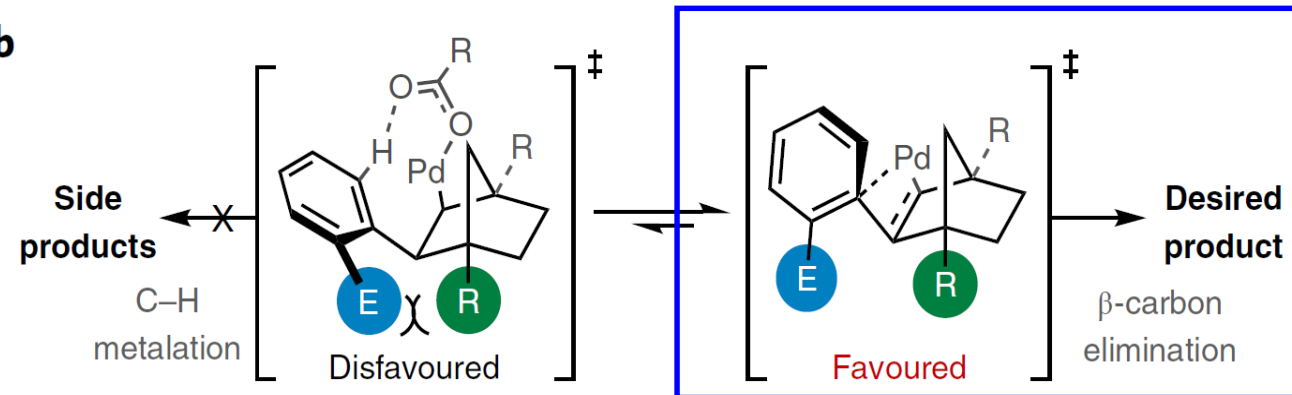
1) (a) Chen, Z.-Y.; Ye, C.-Q.; Zhu, H.; Zeng, X.-P.; Yuan, J.-J. *Chem. Eur. J.* **2014**, 20, 4237.

(b) Wang, J.; Li, R.; Dong, Z.; Liu, P.; Dong, G. *Nat. Chem.* **2018**, 10, 866.

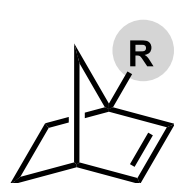
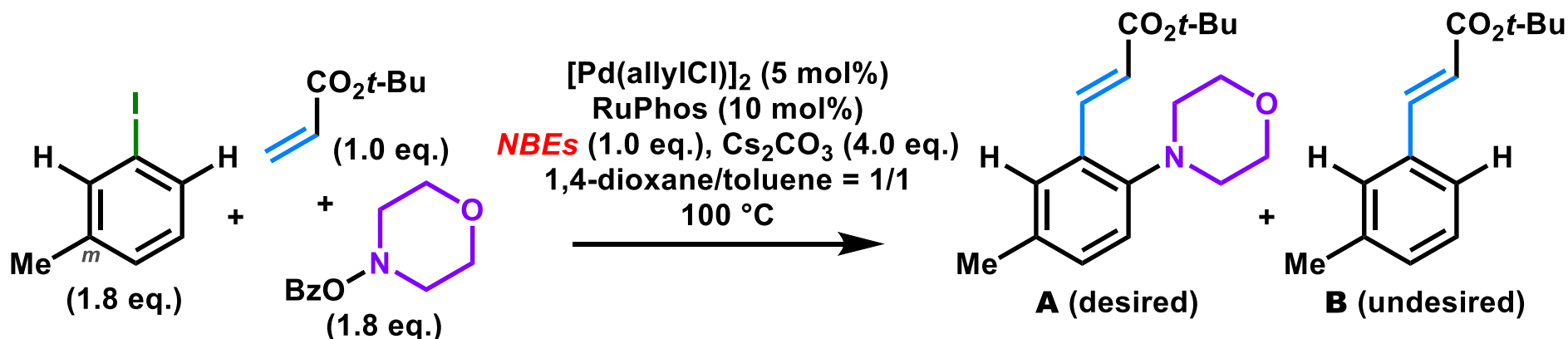
Working Hypothesis¹⁾



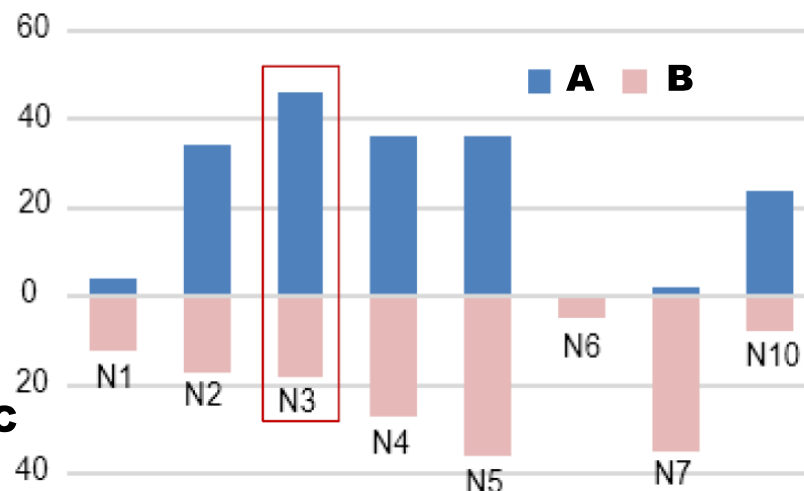
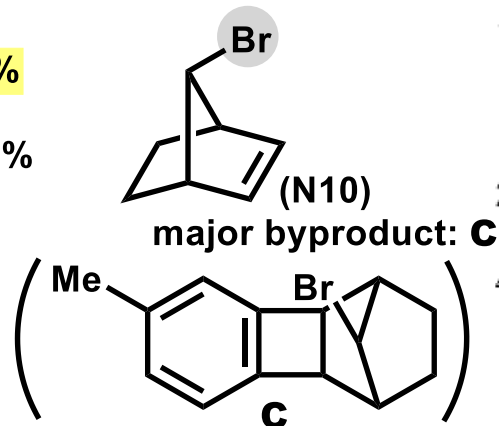
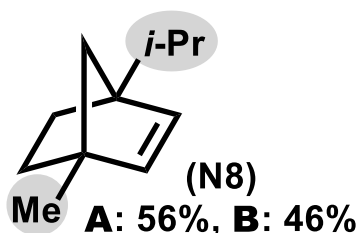
desired product



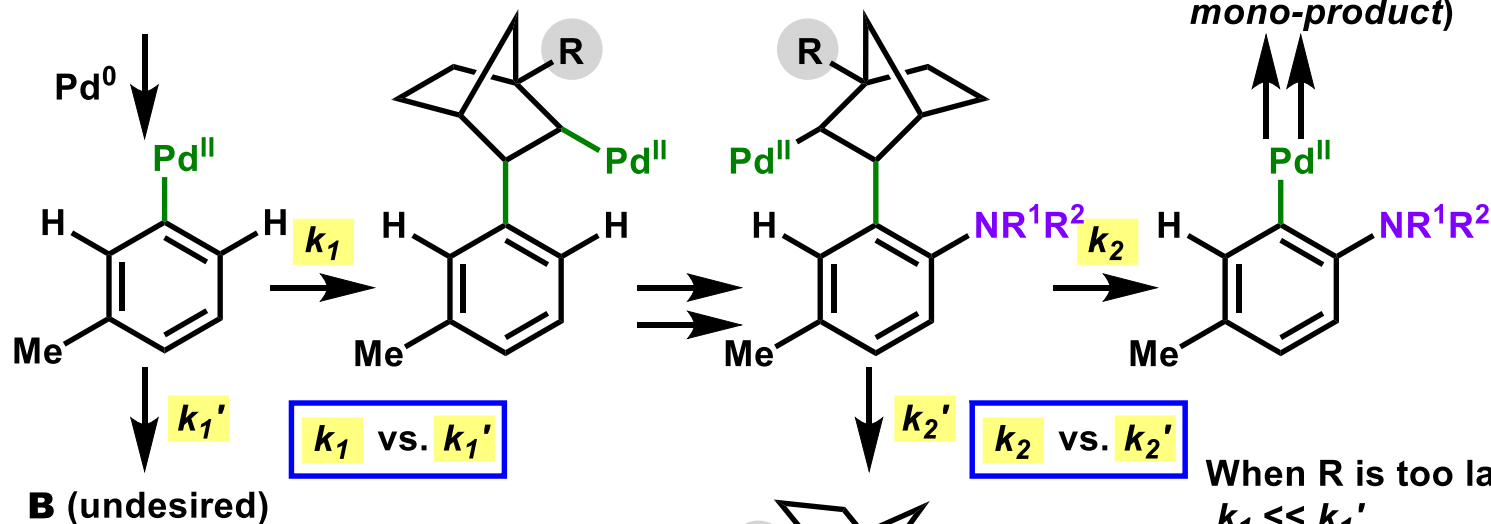
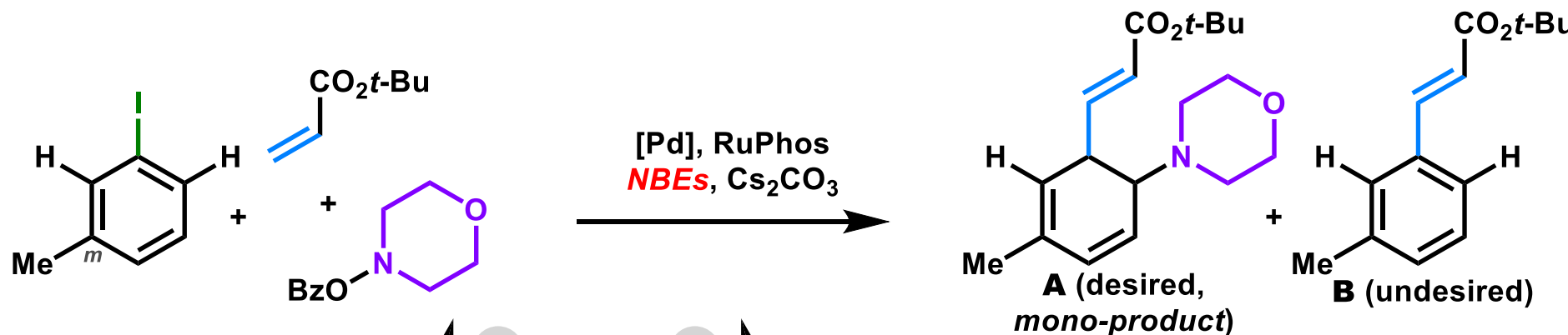
Optimization of Norbornene (NBE) Derivatives¹⁾



R = H (N1); A: <5%, B: 19%
R = Me (N2); A: 54%, B: 25%
R = *n*-C₇H₁₅ (N3); A: 67%, B: 24%
R = Cy (N4); A: 54%, B: 38%
R = *On*-C₄H₇ (N5); A: 58%, B: 24%
R = CO₂Me (N6); A: <5%, B: 7%
R = Ph (N7); A: 6%, B: 38%



Substituents Effect on NBEs¹⁾



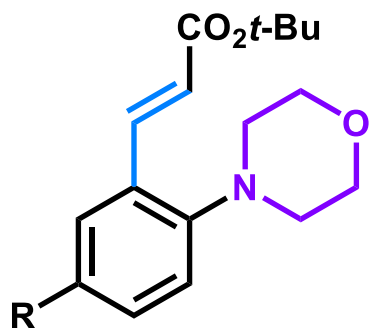
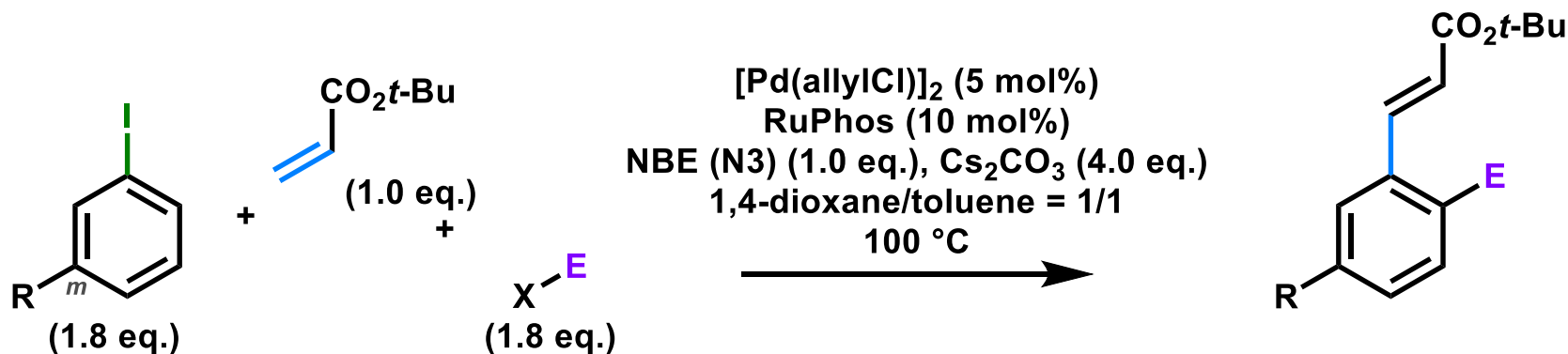
NBEs

$\text{R} = \text{Me}$ (N2); **A**: 54%, **B**: 25%
 $\text{R} = n\text{-C}_7\text{H}_{15}$ (N3); **A**: 67%, **B**: 24%
 $\text{R} = \text{Cy}$ (N4); **A**: 54%, **B**: 38%

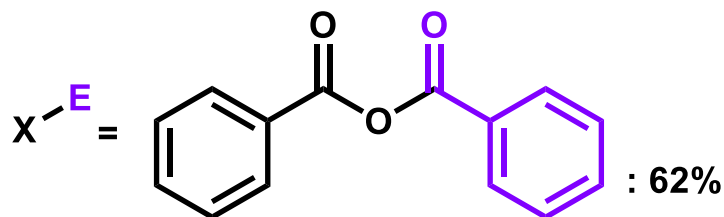
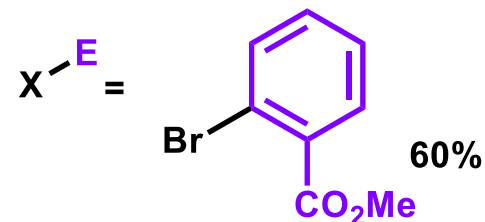
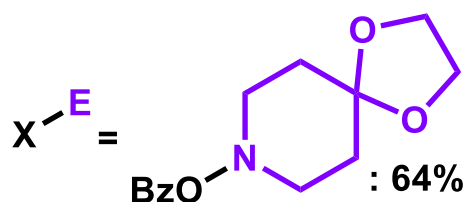
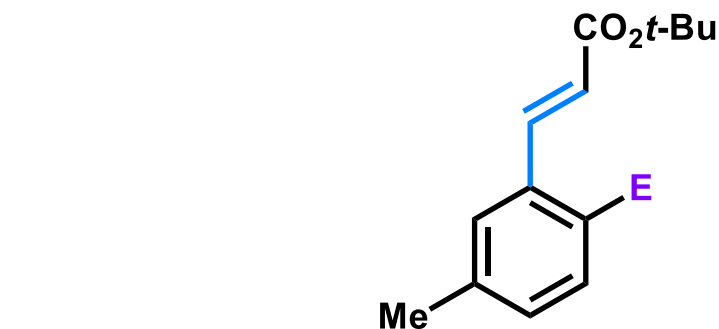
When R is too large ($\text{R} = \text{Cy}$);
 $k_1 \ll k_1'$
 When R is too small ($\text{R} = \text{H}, \text{Me}$);
 $k_2 \ll k_2'$
 i.e. **Moderate bulkiness is important.**

byproducts

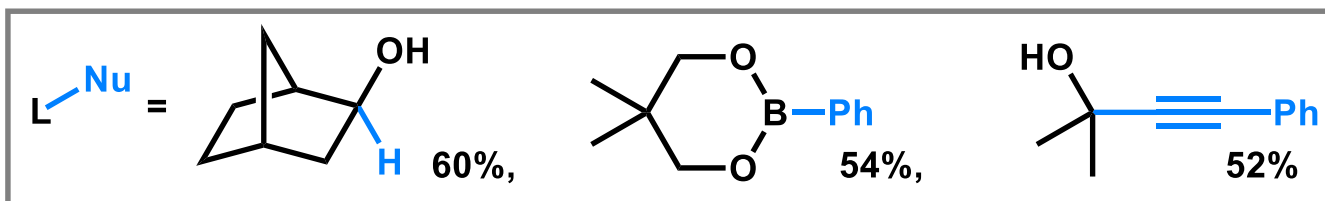
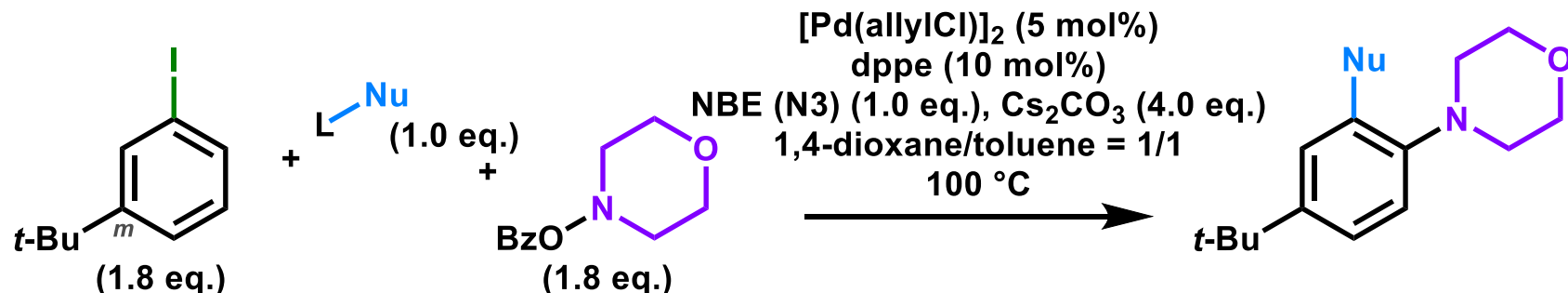
Substrate Scope (1)¹⁾



R = Me: 66%
 R = *i*-Pr: 74%
 R = *t*-Bu: 78%
 R = *Oi*-Pr: 60%
 R = NMe₂: 70%
 R = CO₂Me: 74%
 R = CF₃: 65%
 R = NO₂: 60%

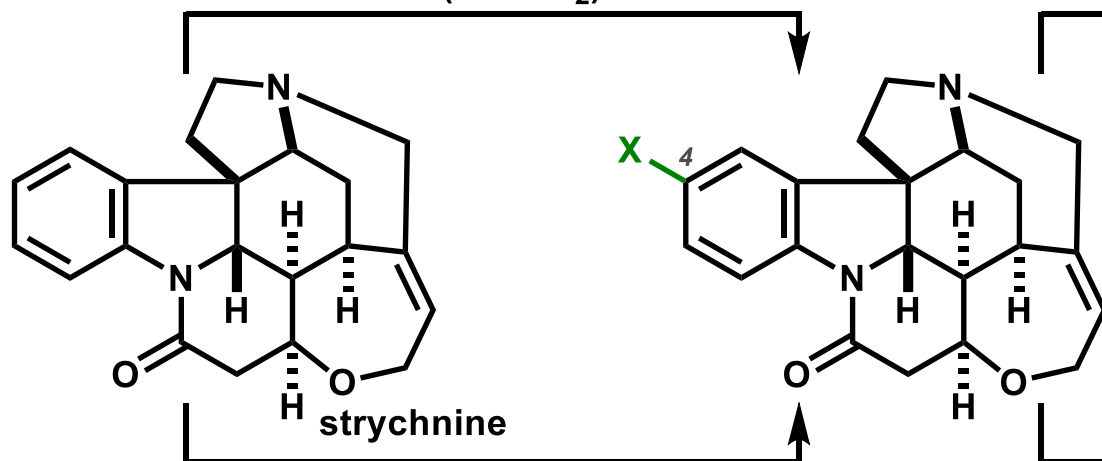


Substrate Scope (2) and Practical Application¹⁾



previous time

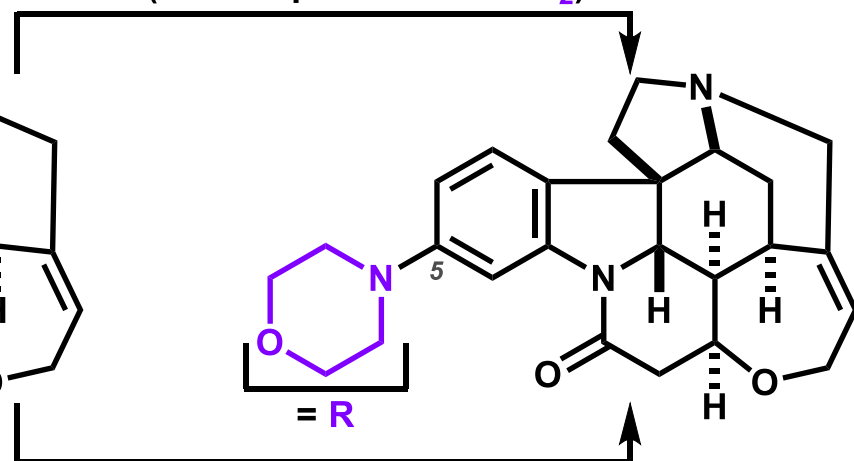
51% over 2 steps
(X = NH₂)



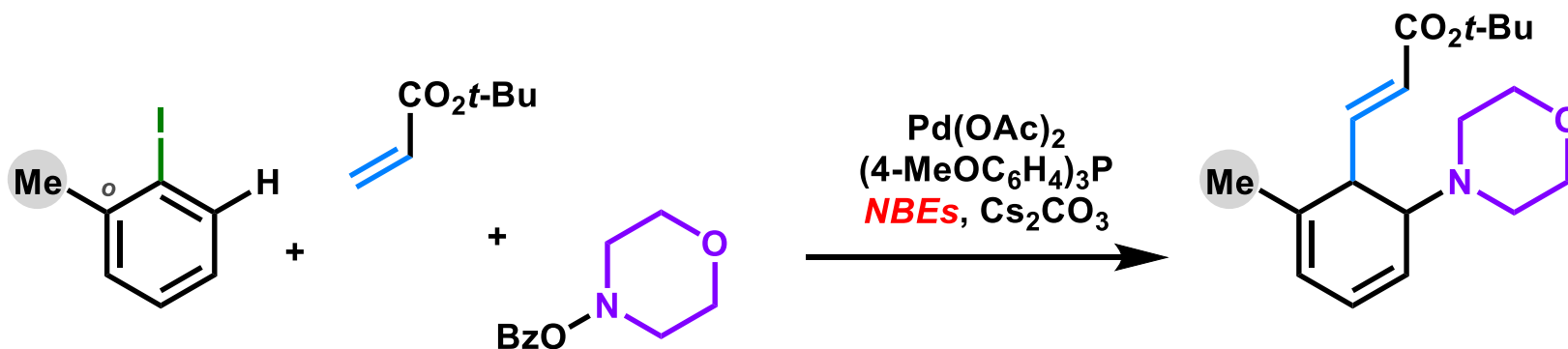
this time

1. C-H iodination (X = I)
88%

35% over 5 steps
(R is displaced with NH₂)



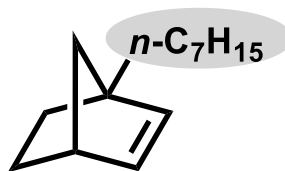
Limitation¹⁾



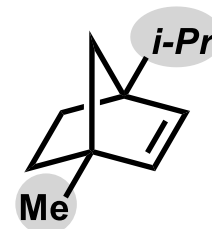
NBES



norbornene
83%



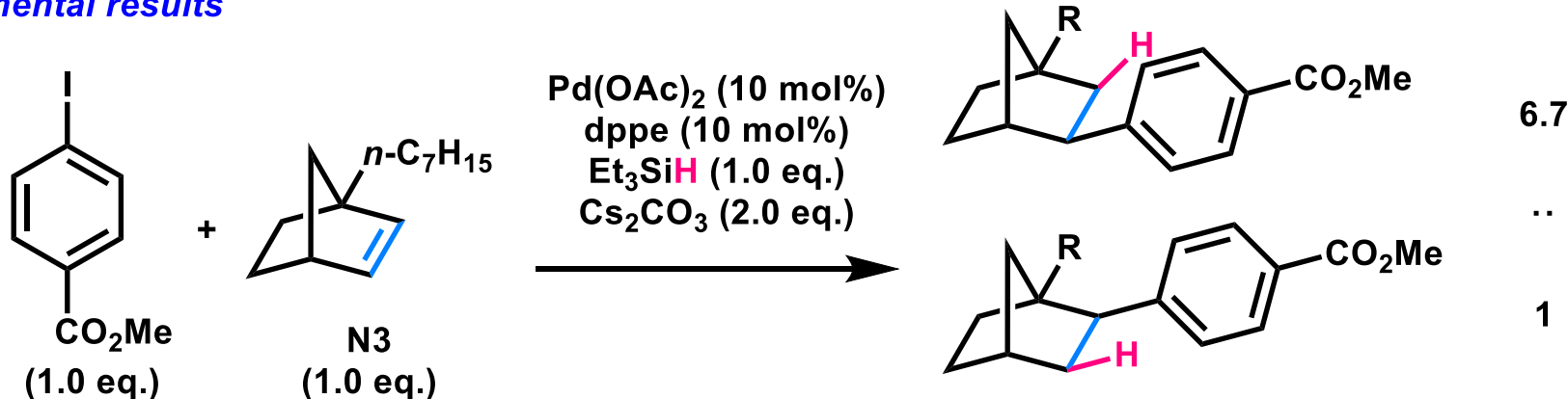
N3
22%



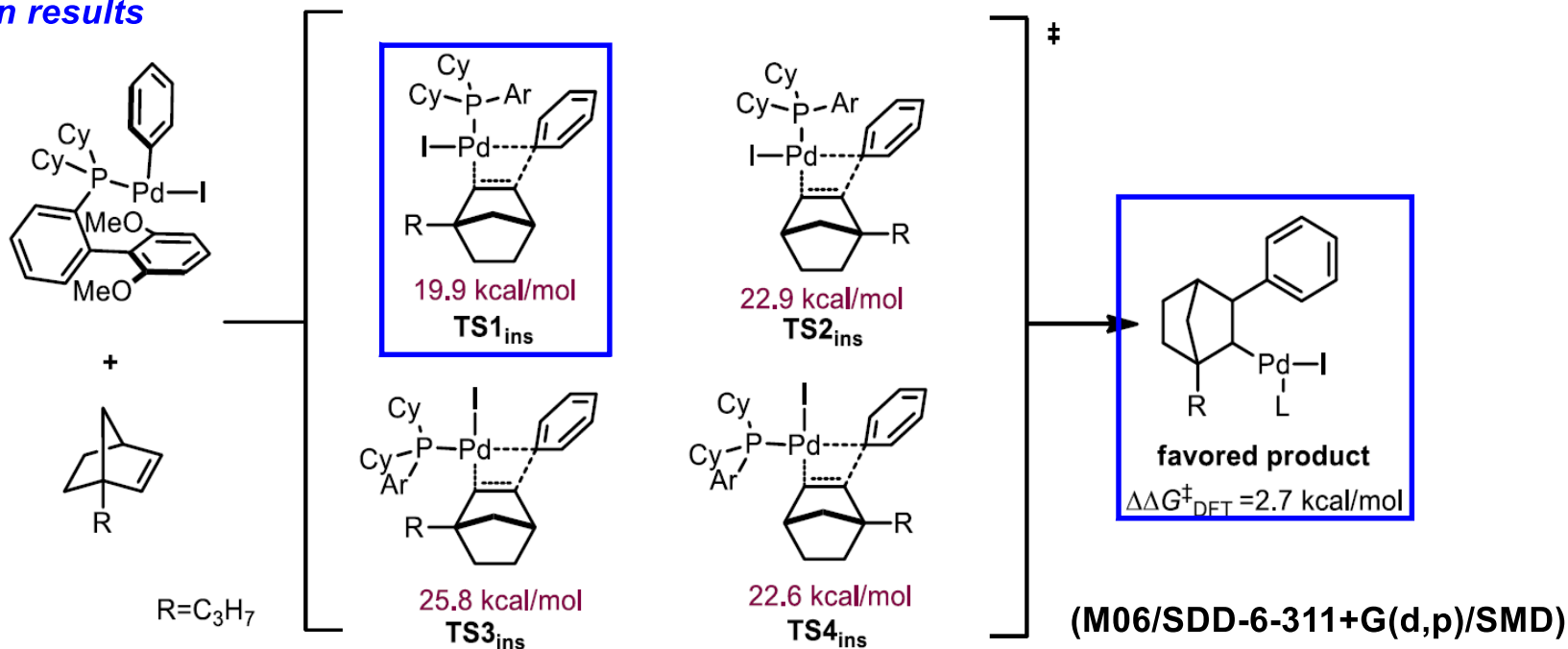
N8
0%

Mechanical Study (1): Selectivity in NBE Insertion¹⁾

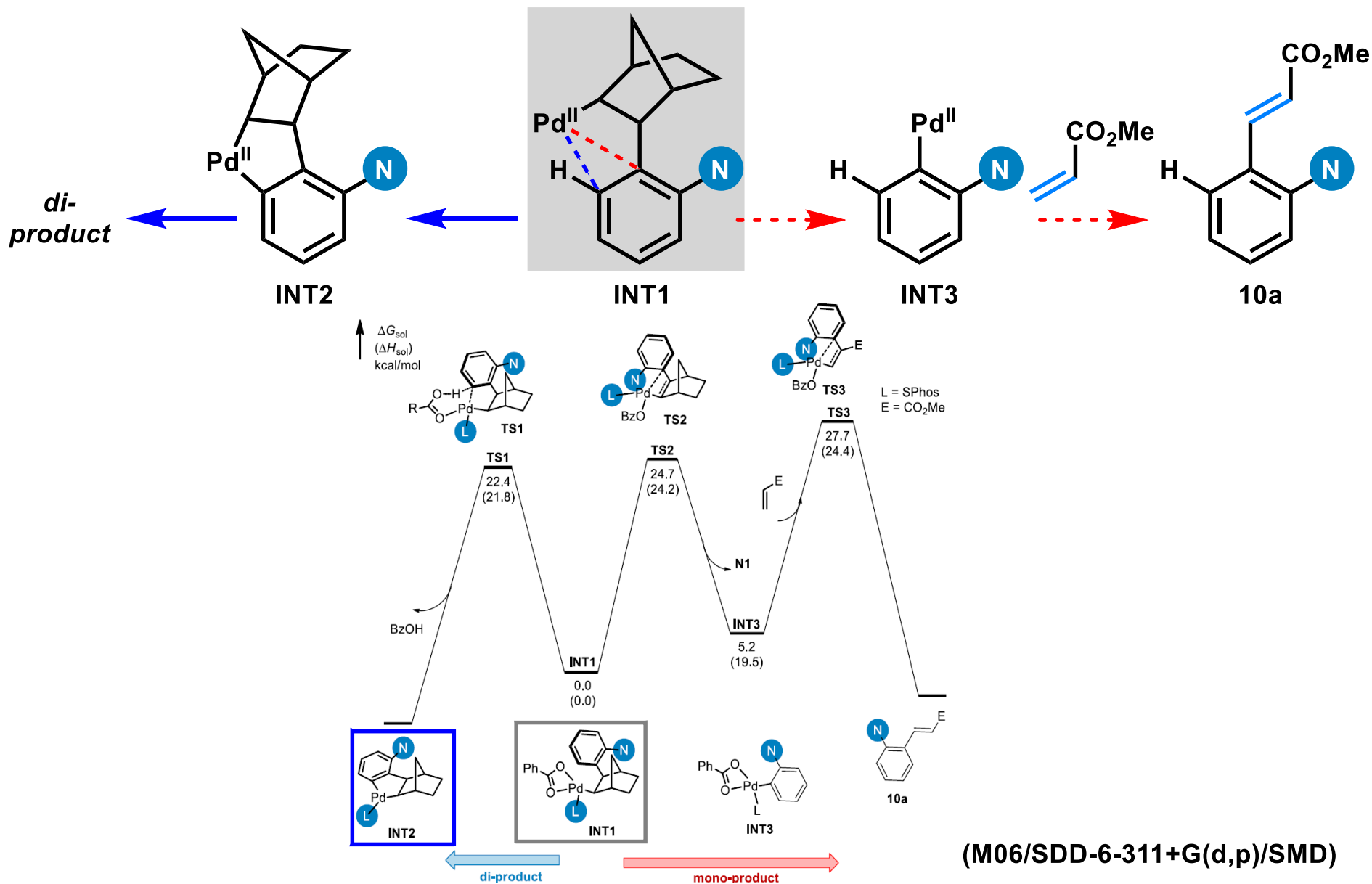
experimental results



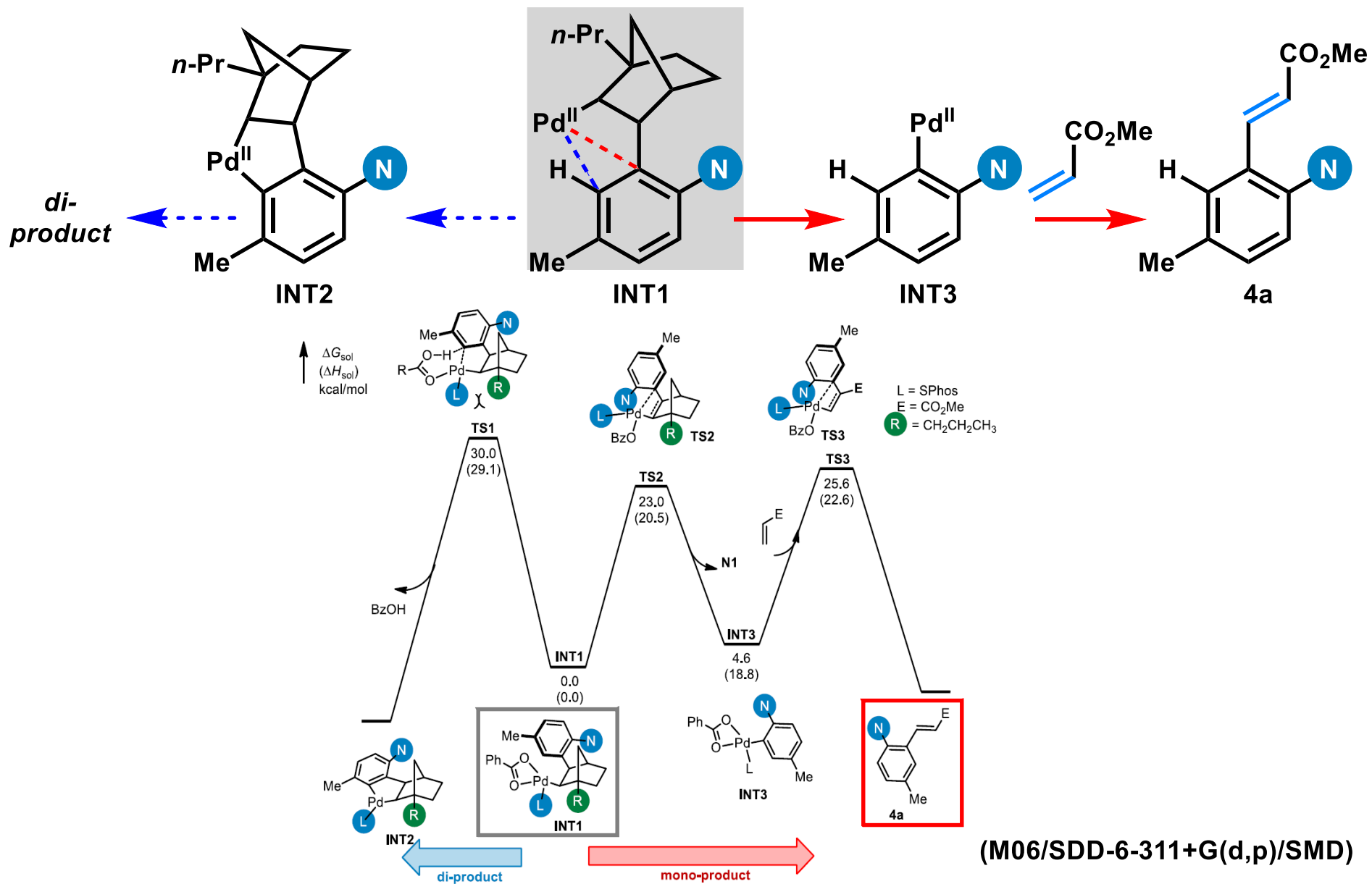
calculation results



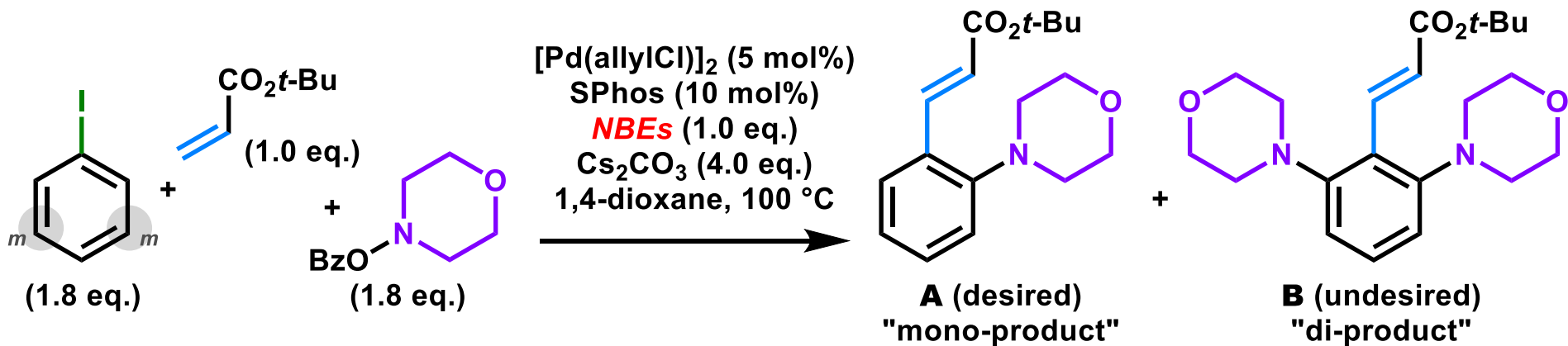
Mechanistic Study (2): Norbornene¹⁾



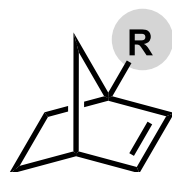
Mechanistic Study (2): Mono-Substituted Norbornene¹⁾



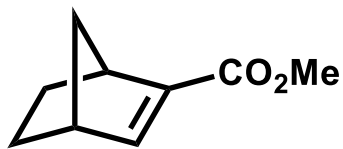
Starting Materials Without Meta-Substituents¹⁾



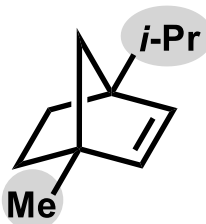
NBEs



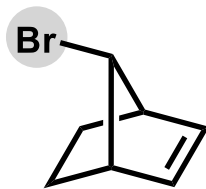
R = H (N1); **A**: 0%, **B**: 29%
 R = $n\text{-C}_7\text{H}_{15}$ (N3); **A**: 2%, **B**: 12%
 R = Cy (N4); **A**: 36%, **B**: 6%



(N9)
A: 0%, **B**: 30%

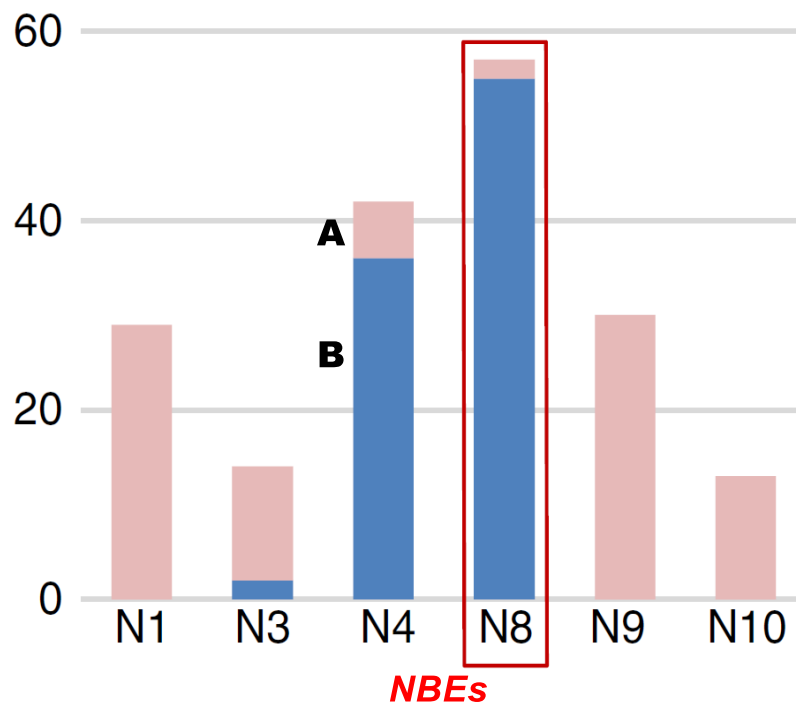


(N8)
A: 55%, **B**: 2%



(N10)
A: 0%, **B**: 13%

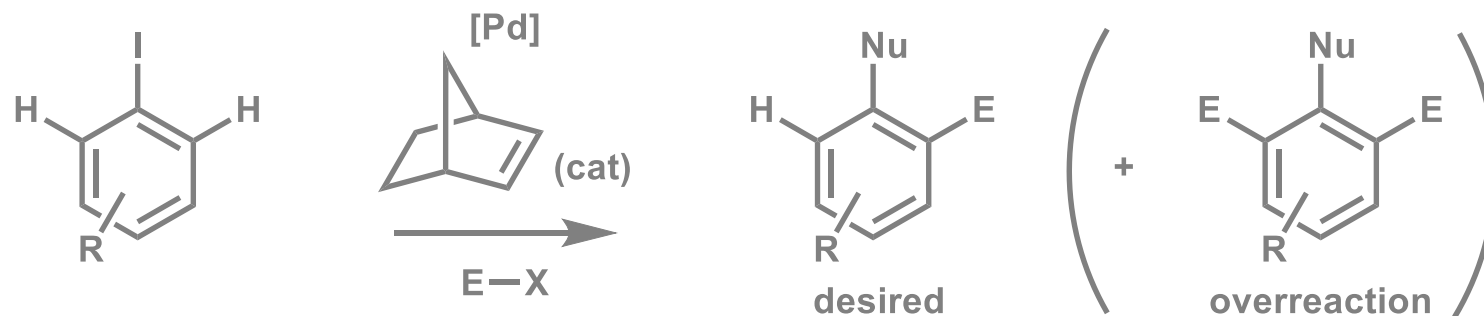
yields (%)



Contents

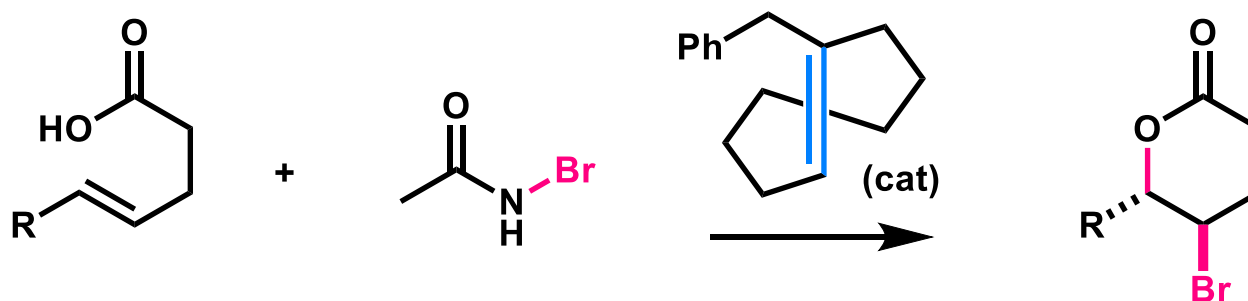
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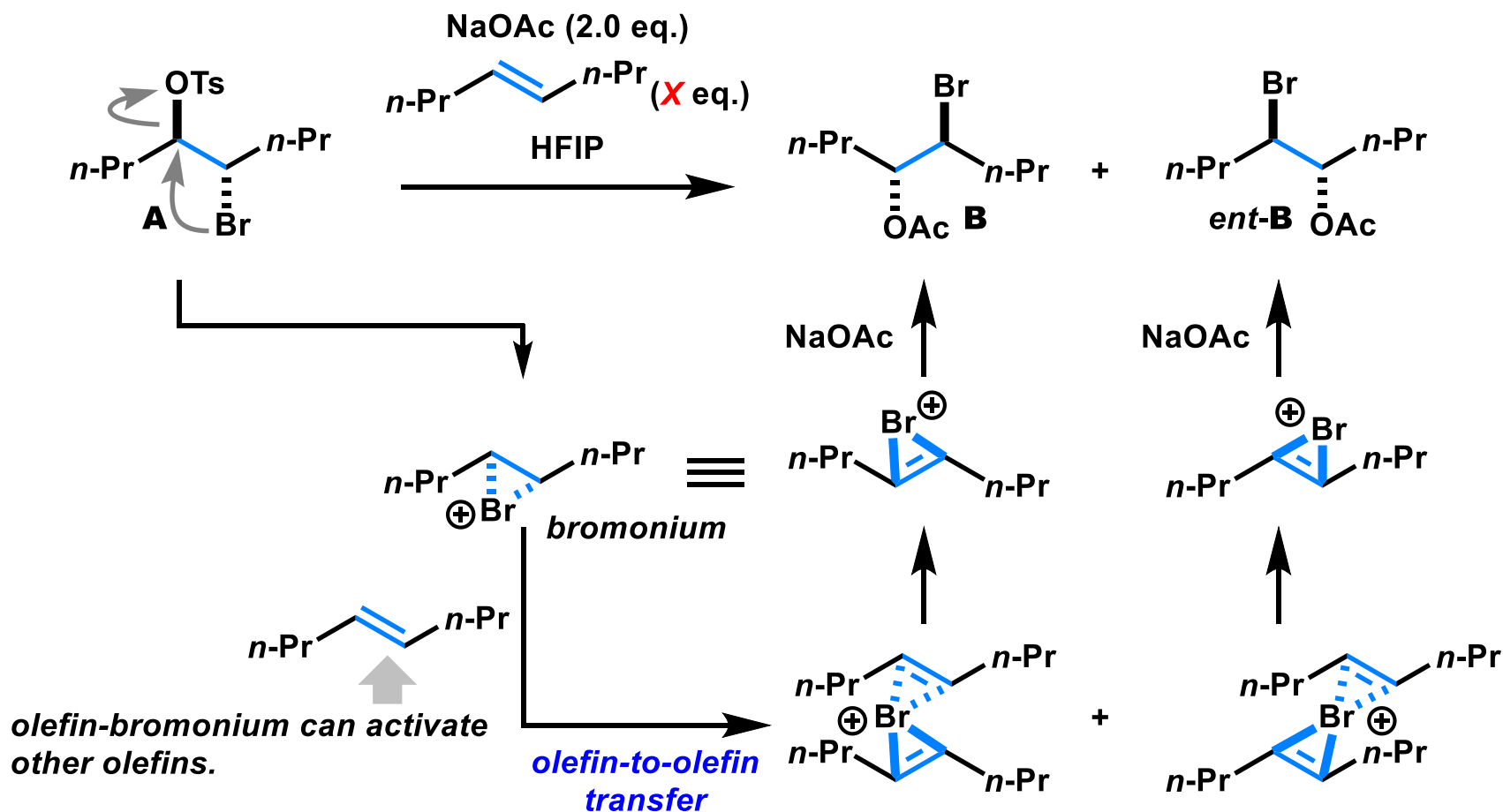


3. *Trans*-Olefin catalysts

Trans-Cyclooctenes as Halolactonization Catalyst (Matsubara, 2018)

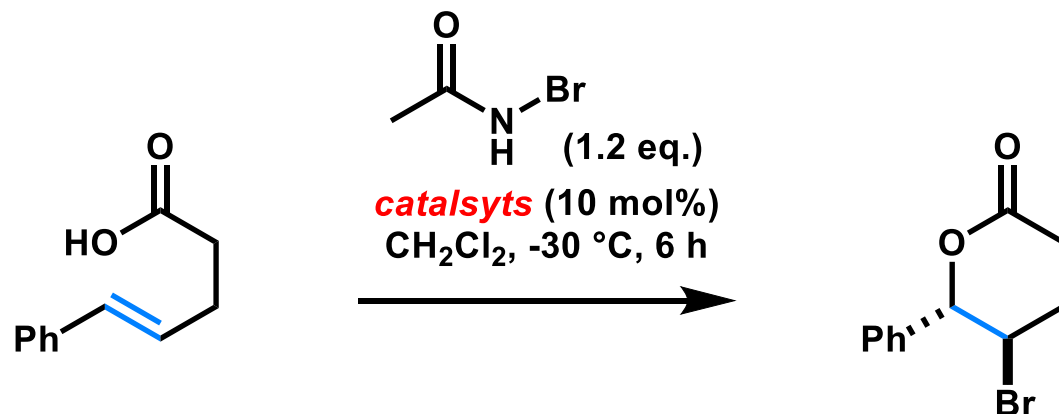


Olefin-to-Olefin Transfer of Bromonium¹⁾



entry	$n\text{-Pr}-\text{CH}=\text{CH}-\text{n-Pr}$	B : <i>ent</i> - B
1	0 eq.	100 : 0
2	1.0 eq.	64 : 36

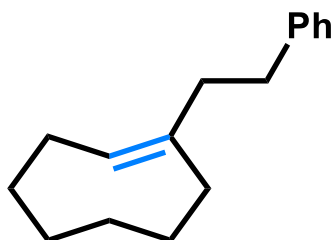
Olefin-Catalysts for Bromolactonization¹⁾



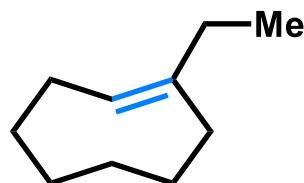
catalysts

without
catalysts

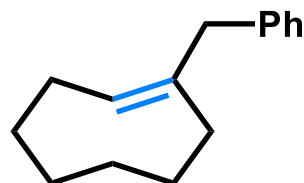
1%



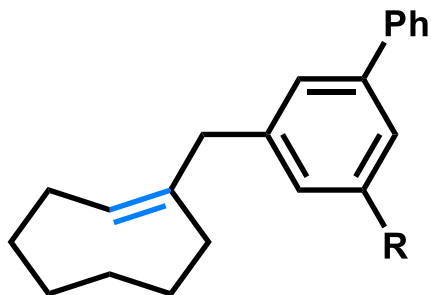
2%



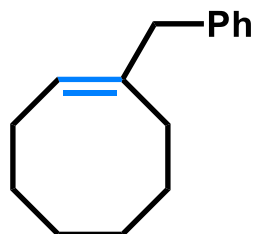
4%



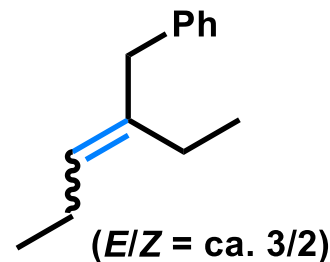
88% (99%^a) ^a Reaction time is 12 h.



R = H: 59%
 R = Ph: 4%

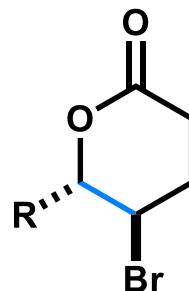
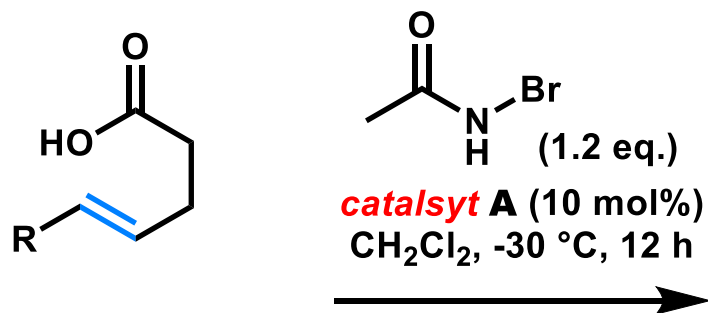


1%



2%

Substrate Scope¹⁾



catalyst A

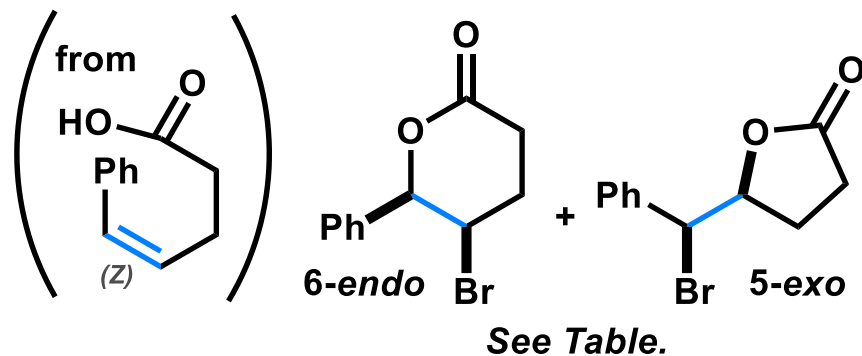
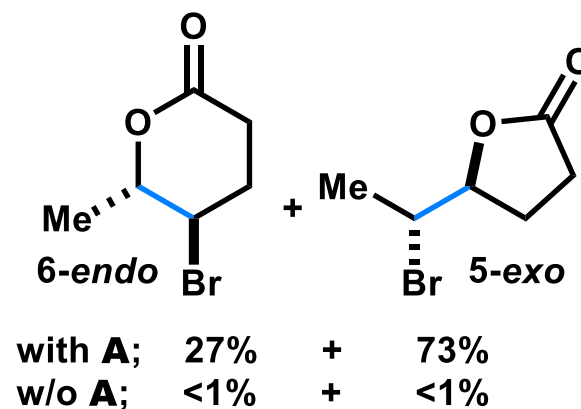
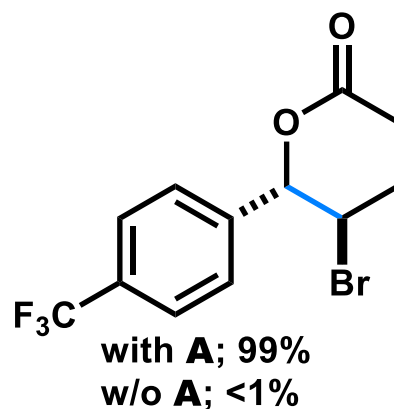
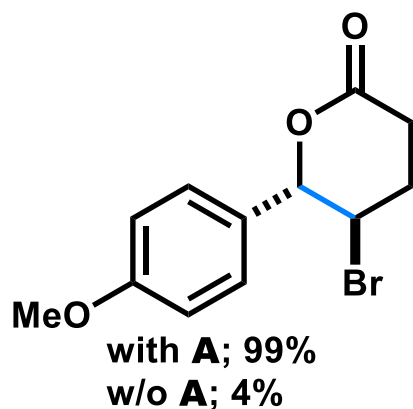
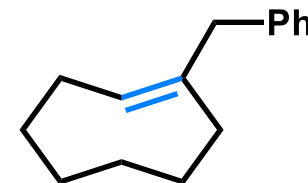
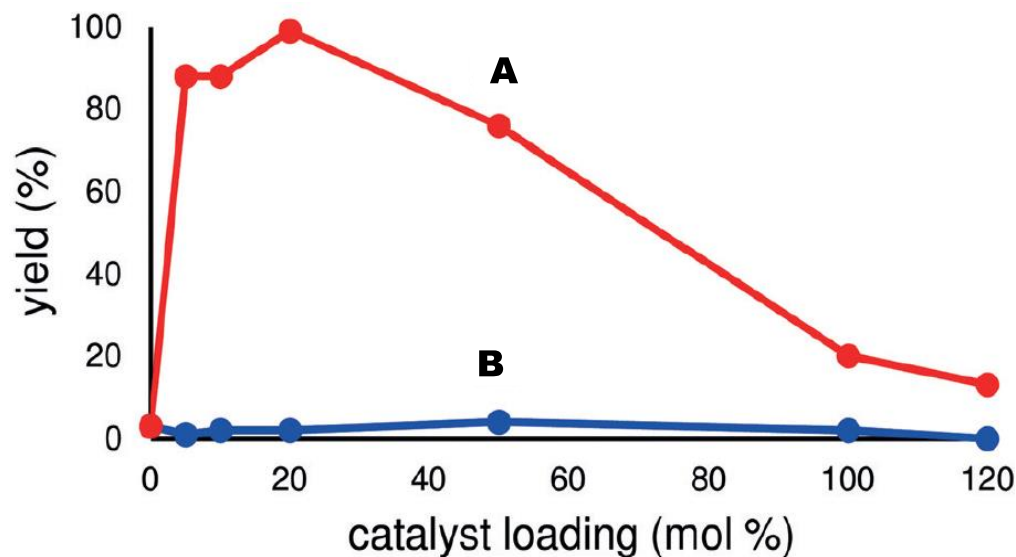
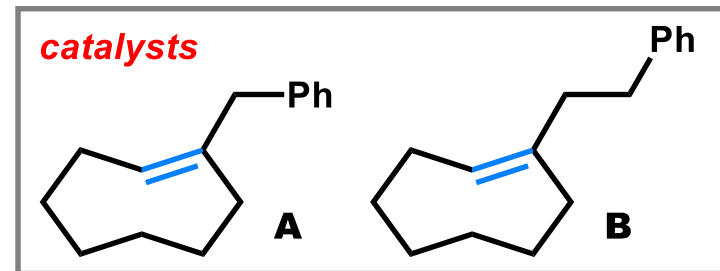
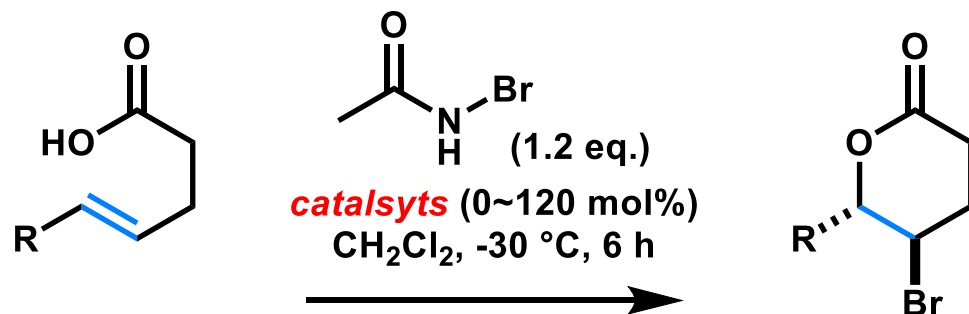


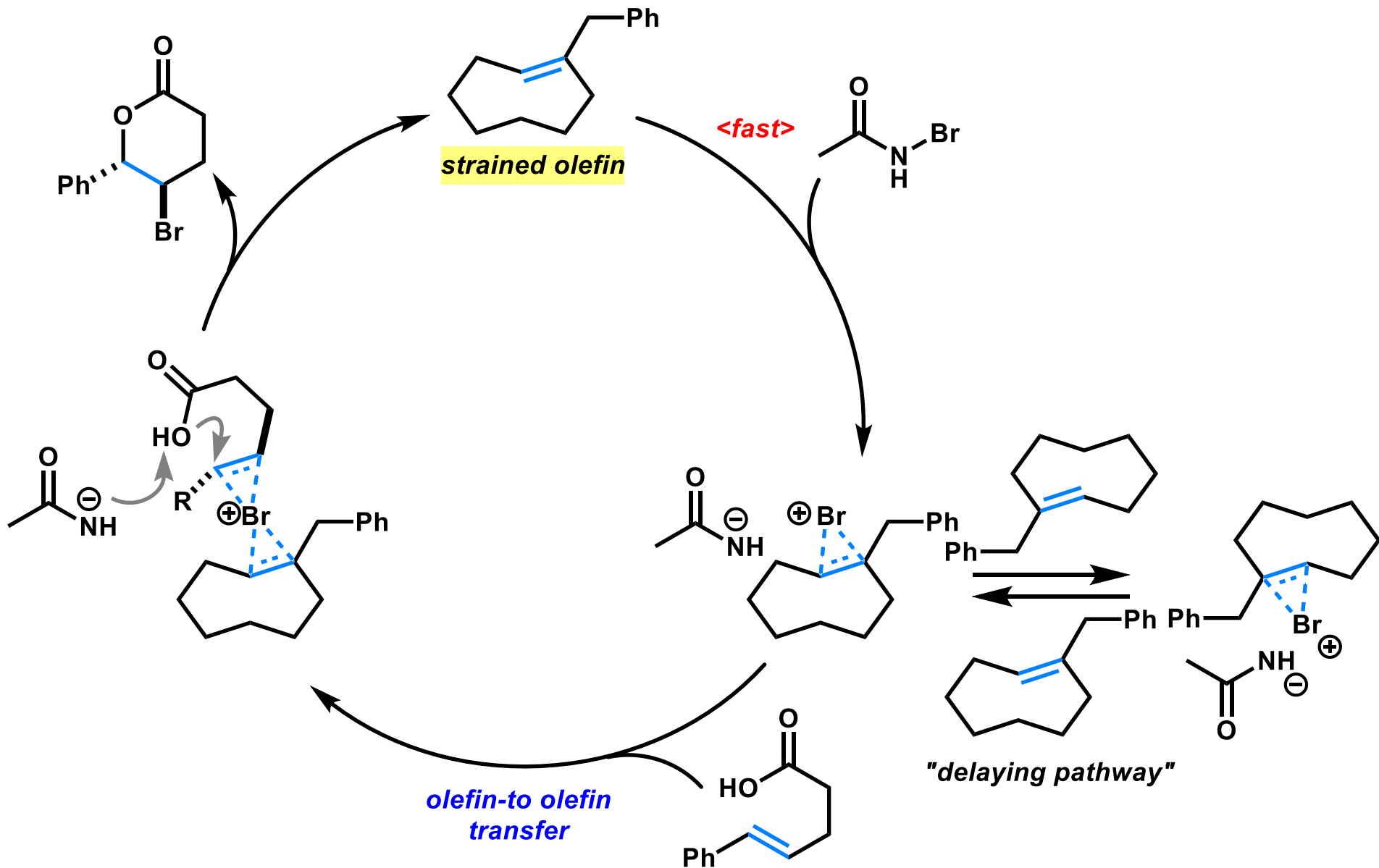
Table.

entry	catalysts	6-endo	5-exo
1	A	26%	71%
2	Et_3N	<1%	89%
3	Ph_3P	15%	69%
4	w/o catalysts	<1%	2%

Effects of Catalyst Loadings¹⁾



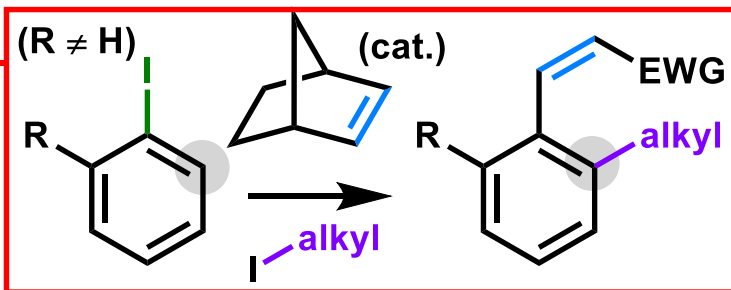
Proposed Reaction Mechanism¹⁾



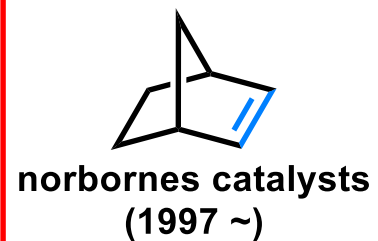
Summary

1997~
start

Catellani



now matured
-> "red ocean"

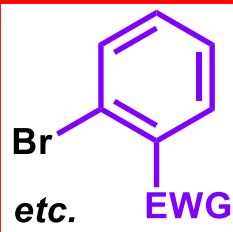


a lot of

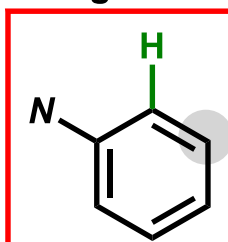
2004~
electrophile expansion

nucleophile expansion

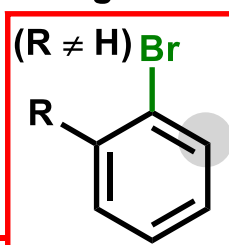
2005~



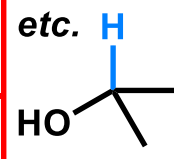
Dong



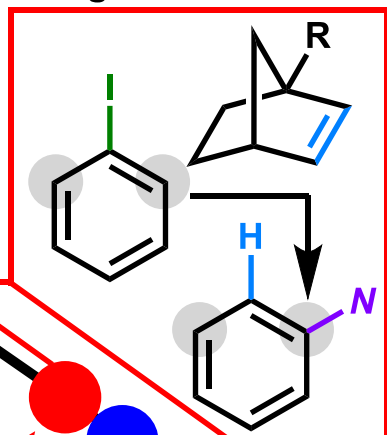
Dong



a lot of
etc.



Dong



2013~

SM expansion

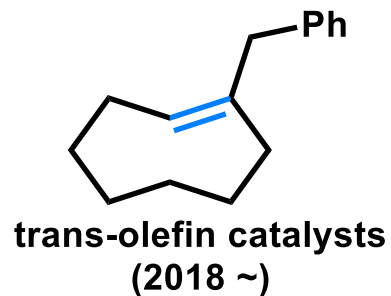
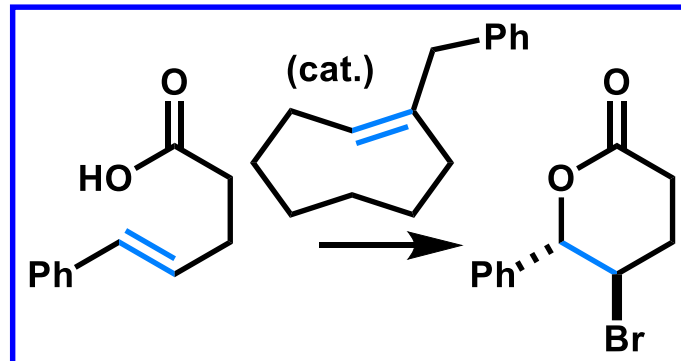
practical improvement

start

2018~

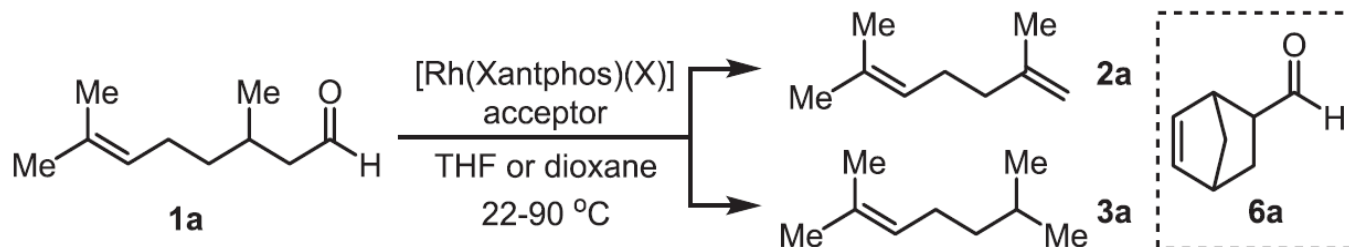
immatured
-> "blue ocean?"

Matsubara

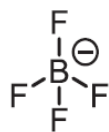


Appendix

Optimization for Reaction Conditions¹⁾



counterions (yield, **2a:3a**): 10% catalyst, 1.2 equiv nbd, dioxane, 90 °C, 1h



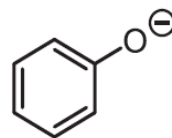
4a
0%



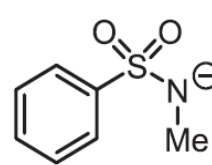
4b
0%



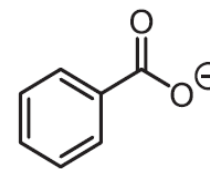
4c
6%, 85:15



4d
27%, 98:2



4e
27%, 98:2



4f
99%, >99:1

acceptors (yield, **2a:3a**): X = 3-OMeBzO⁻, 1.2-3 equiv acceptor, THF, 22-80 °C



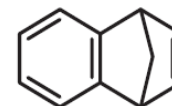
5a, nbd
88%, >99:1
0.3% [Rh], 80 °C



5a, nbd
99%, >99:1
1% [Rh], 60 °C

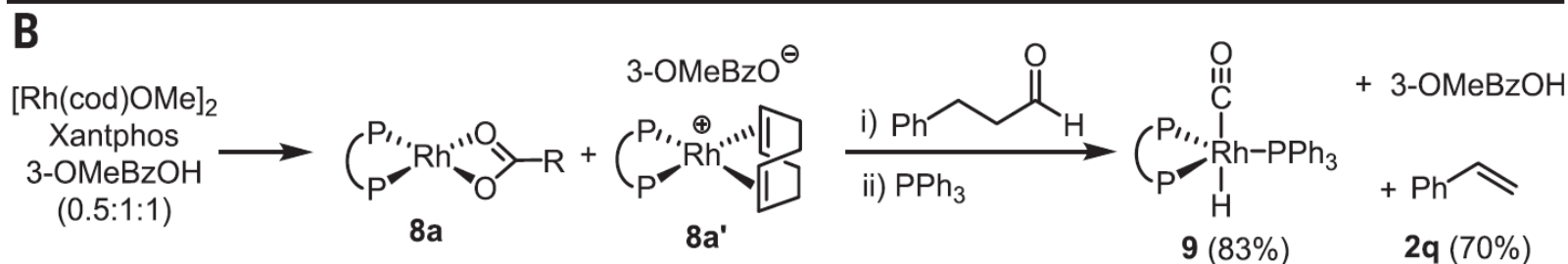
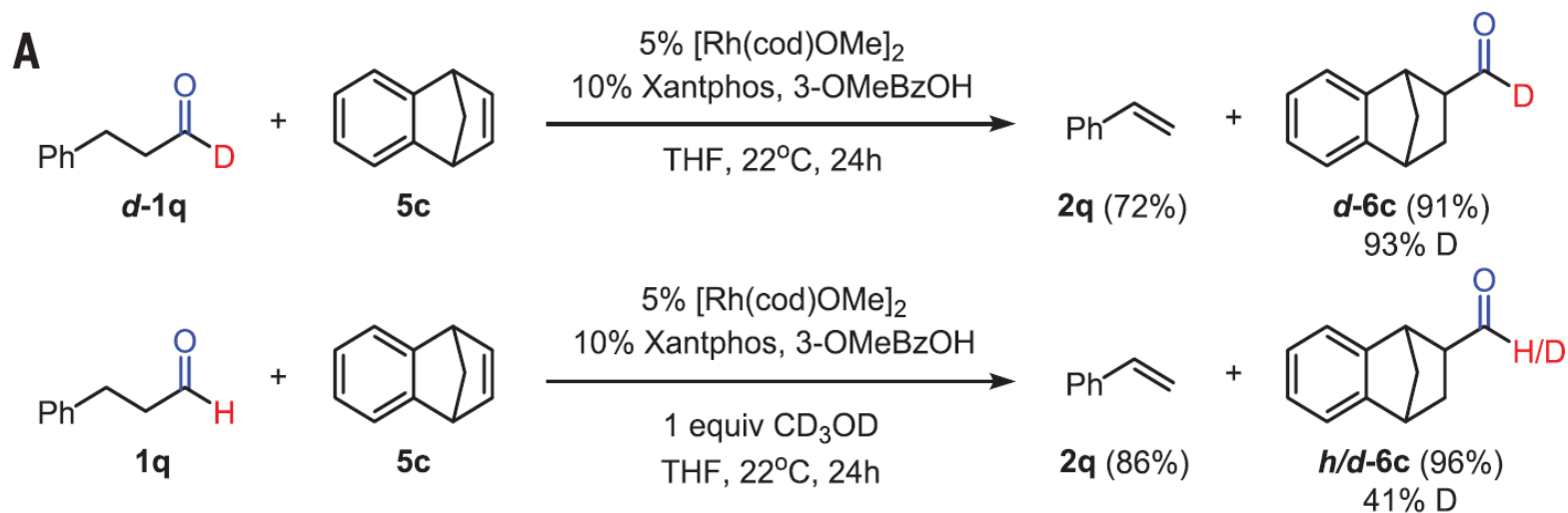


5b, nbe
97%, 99:1
2% [Rh], 40 °C



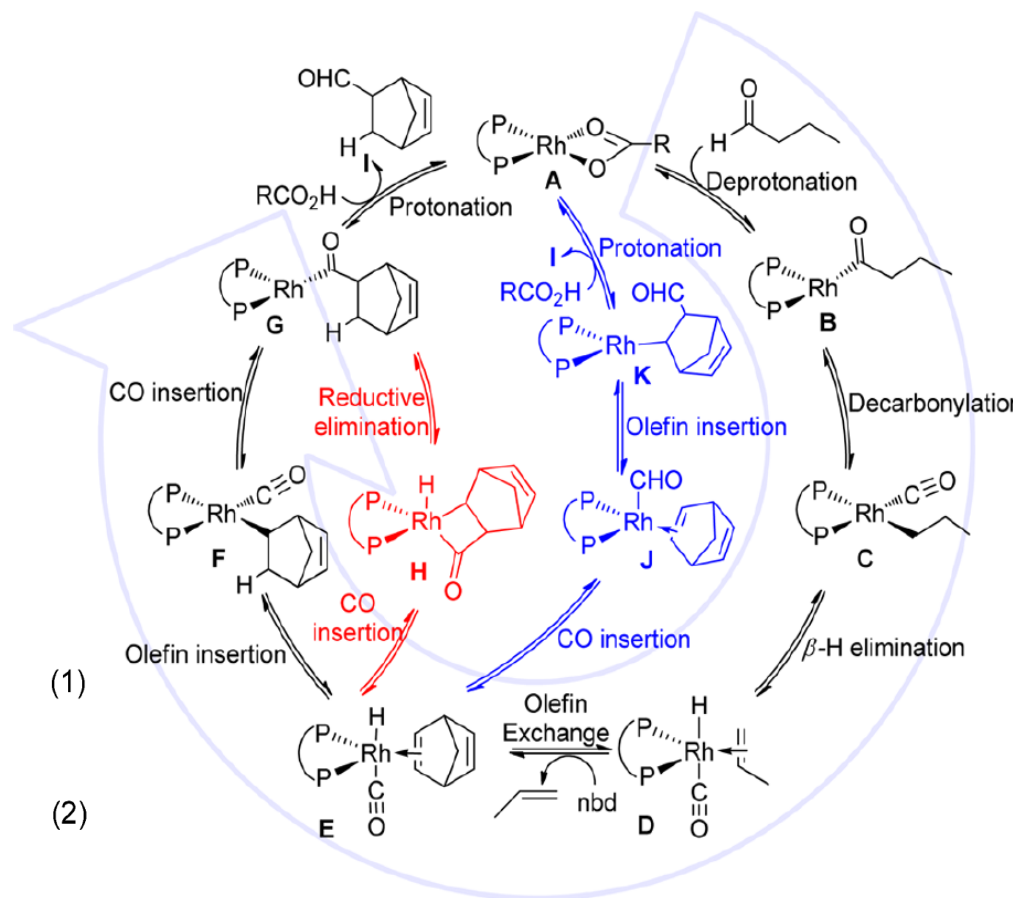
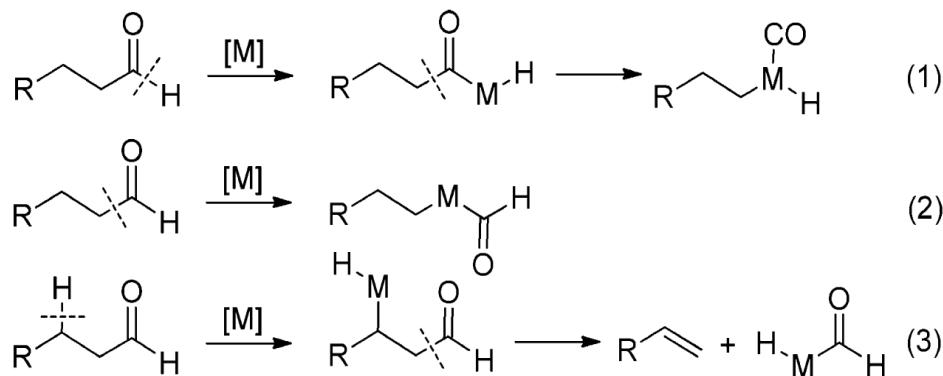
5c, bnbd
99%, 99:1
2% [Rh], 22 °C

Mechanistic Studies¹⁾

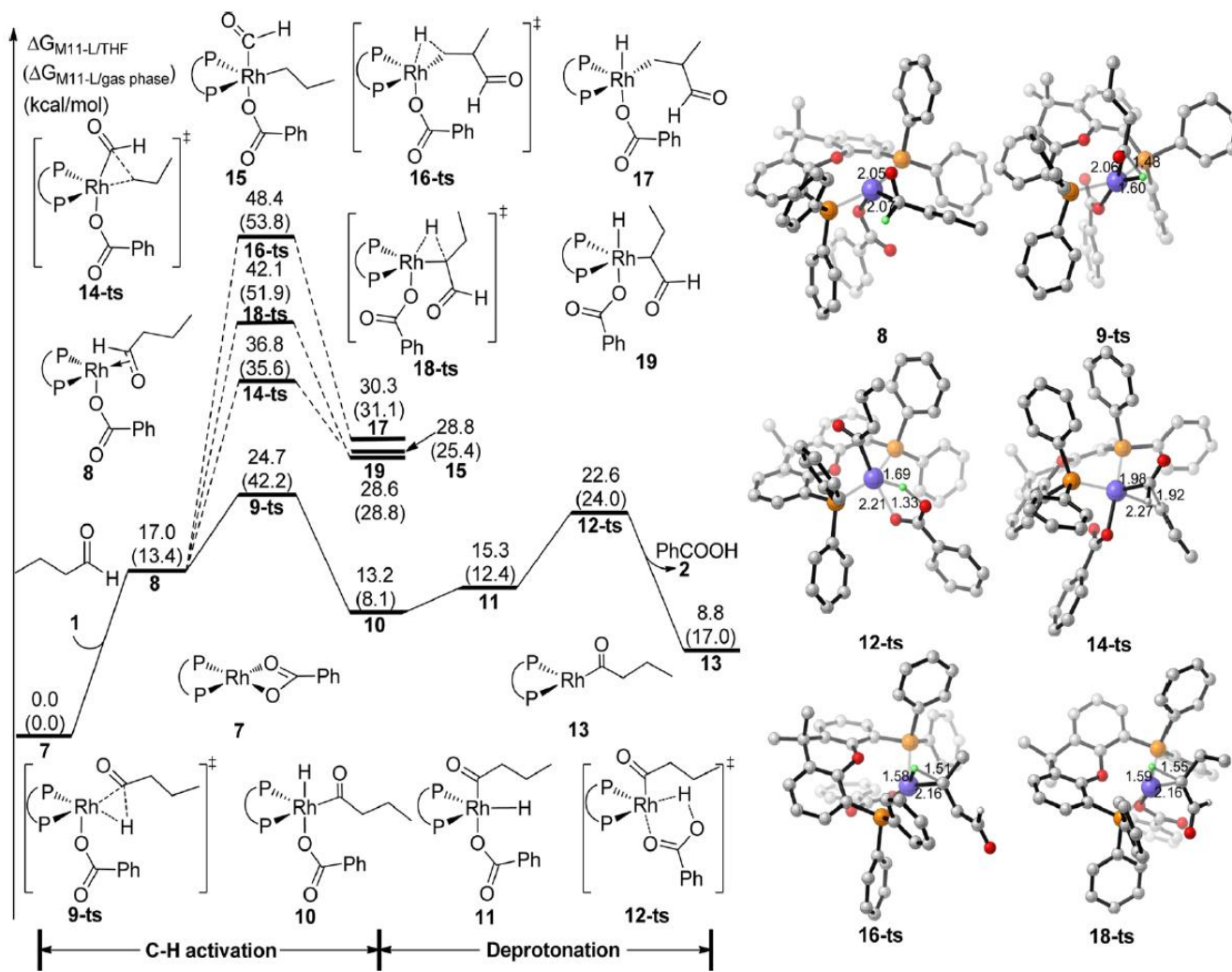


Possible Reaction Pathways¹⁾

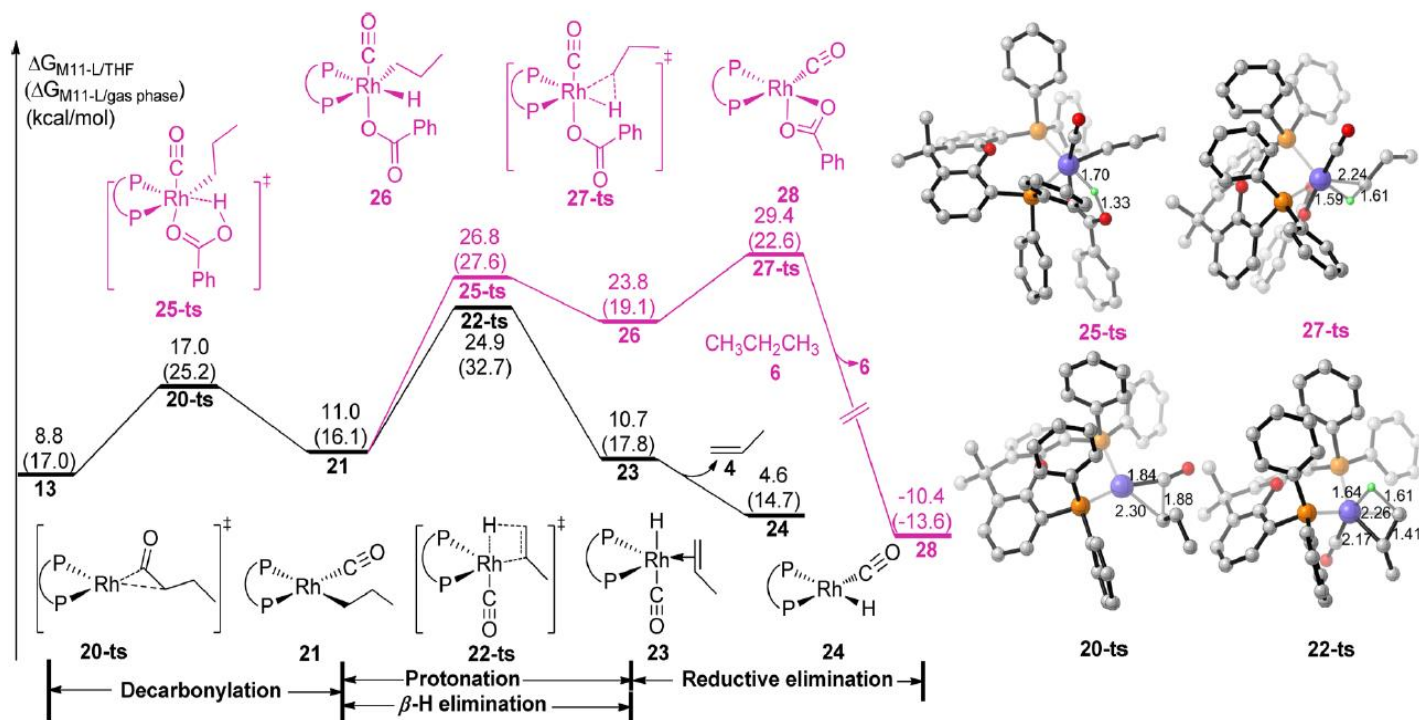
Scheme 2. Possible Modes for Formyl Activation



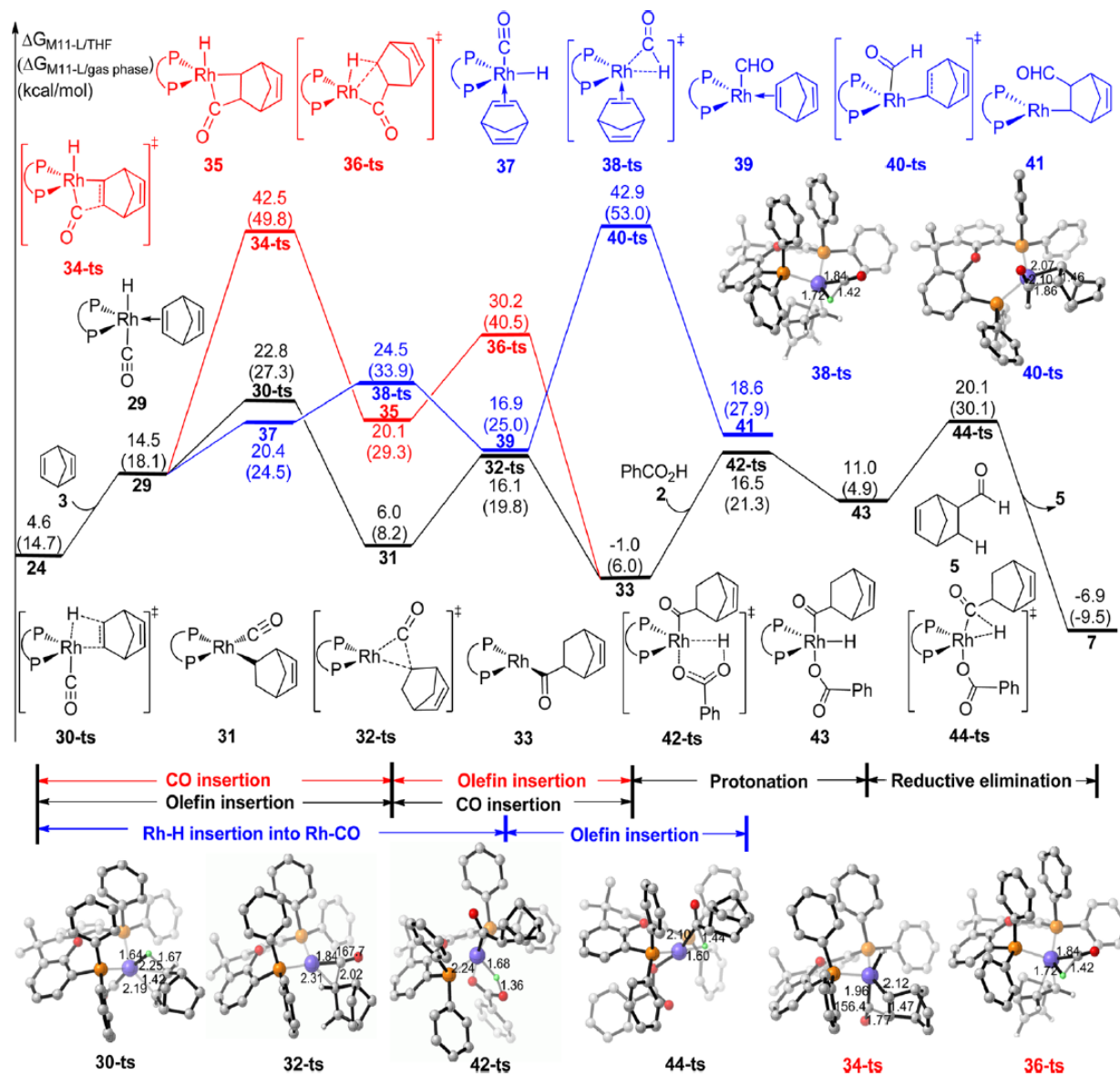
DFT Calculation (1)¹⁾



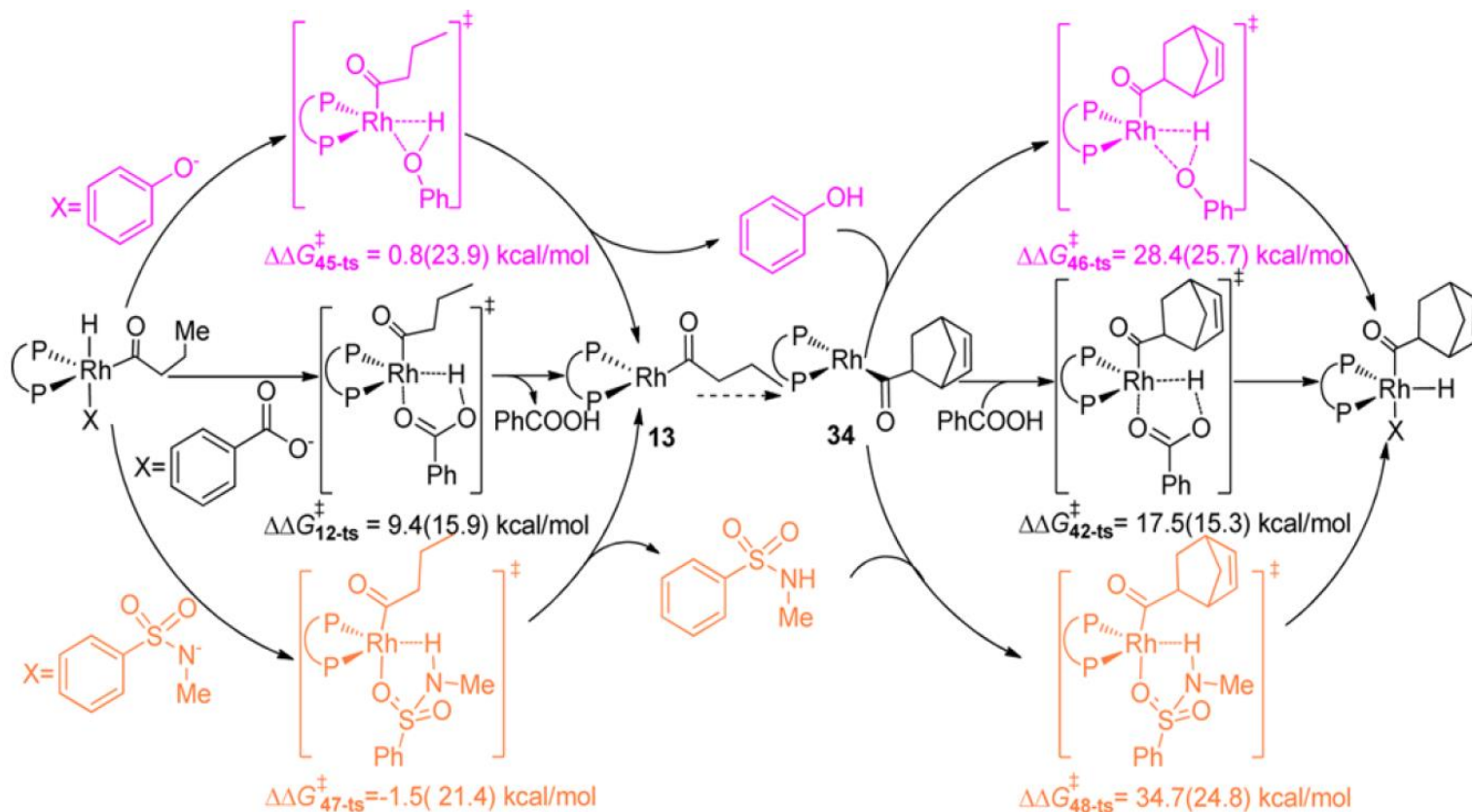
DFT Calculation (2)¹⁾



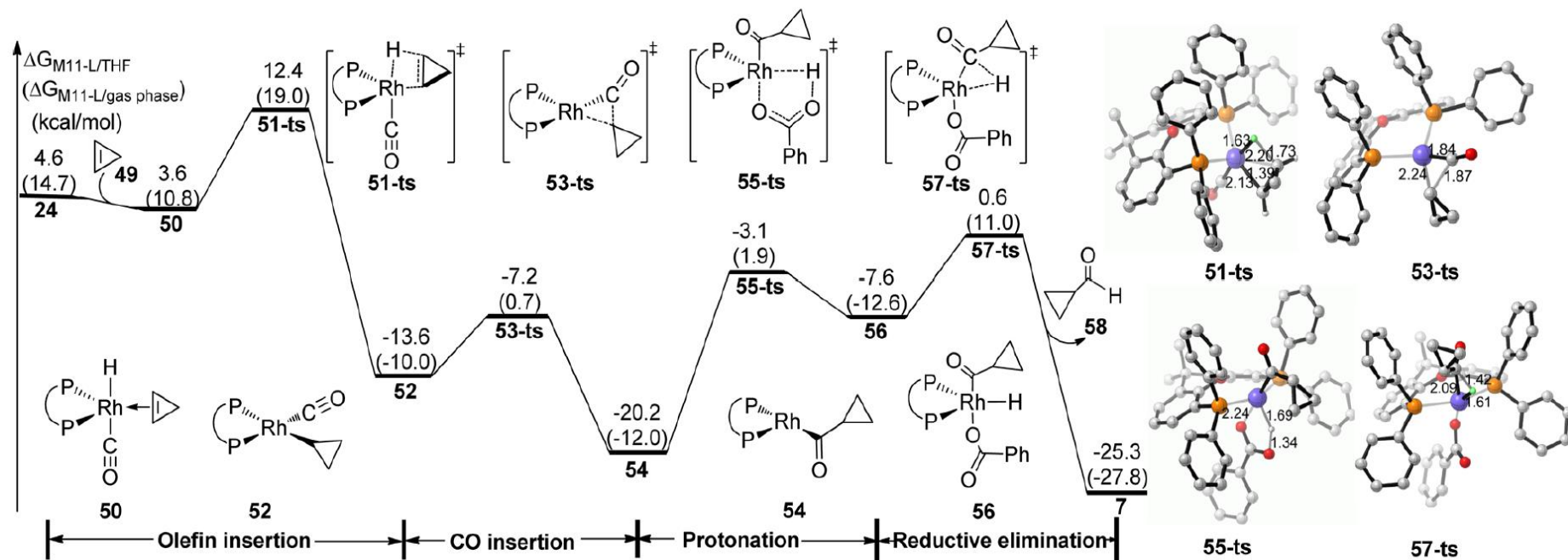
DFT Calculation (3)¹⁾



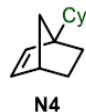
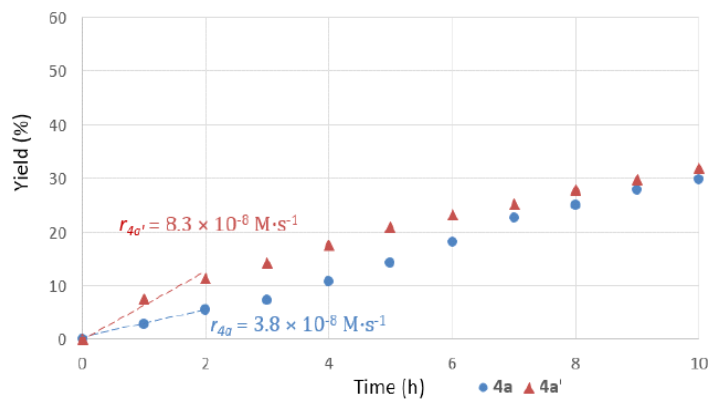
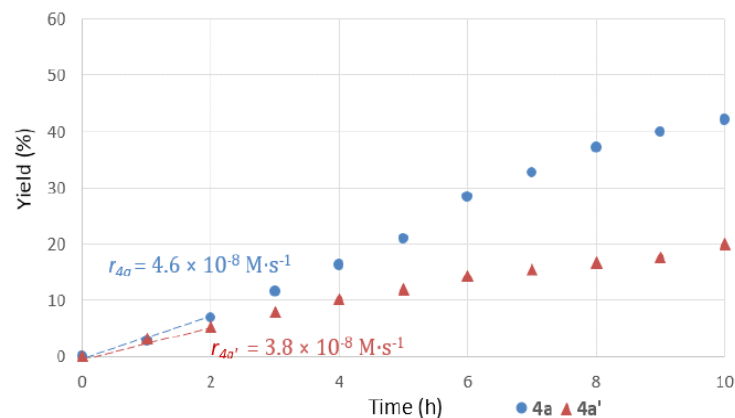
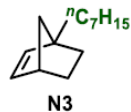
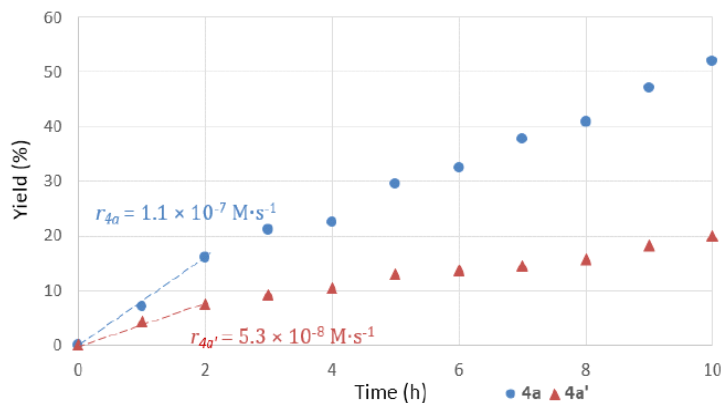
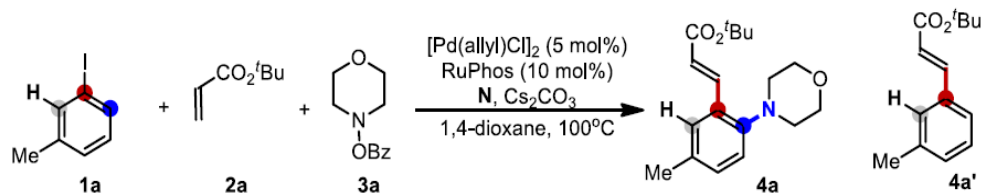
Counter Anion Effect¹⁾



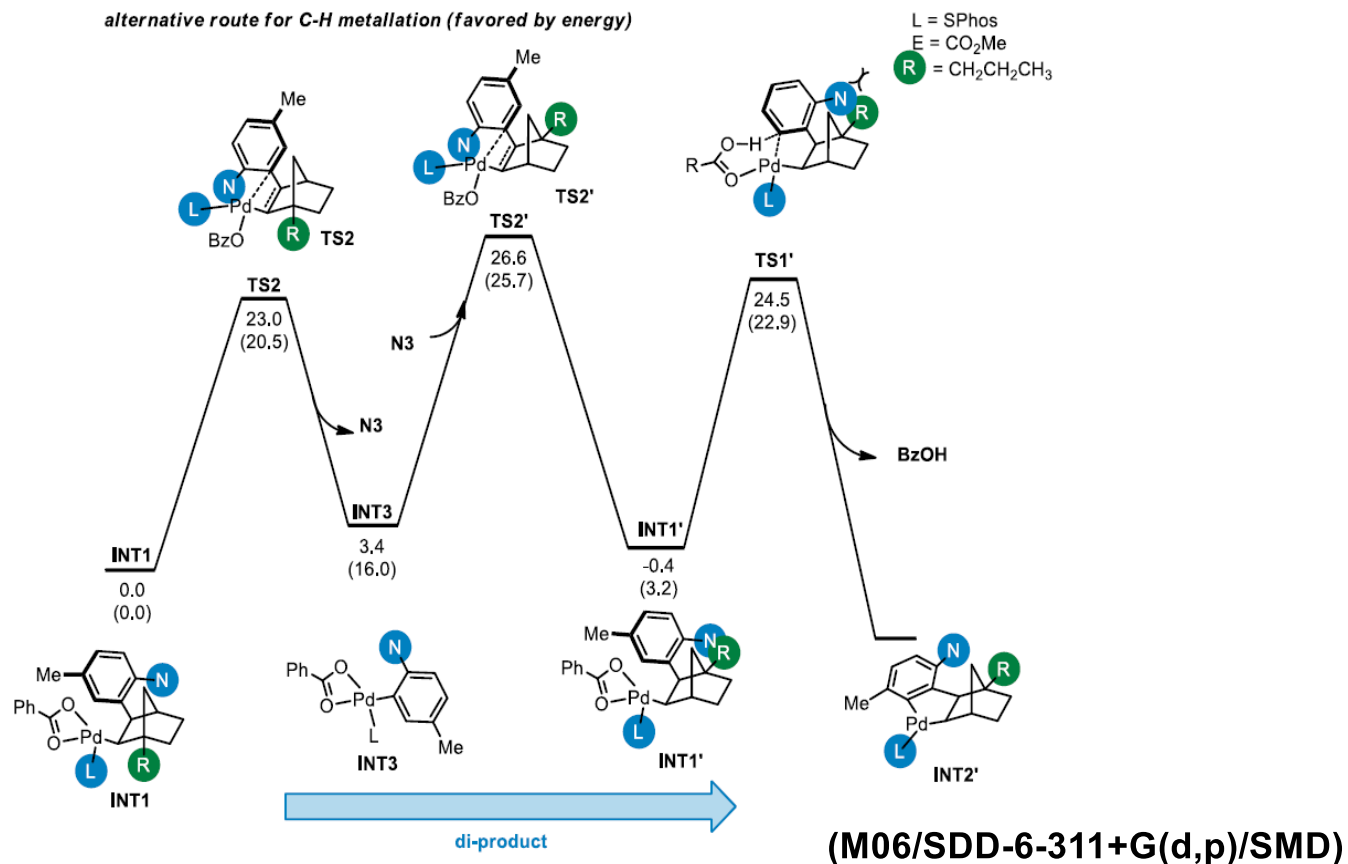
Cyclopropene System¹⁾



Kinetic Effect¹⁾



DFT Calculation¹⁾



Preparation of Catalysts¹⁾

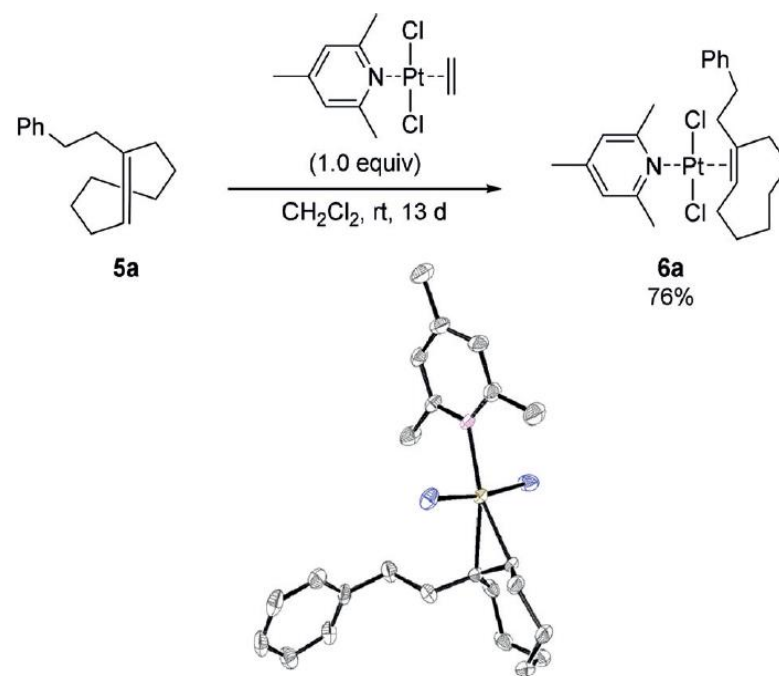
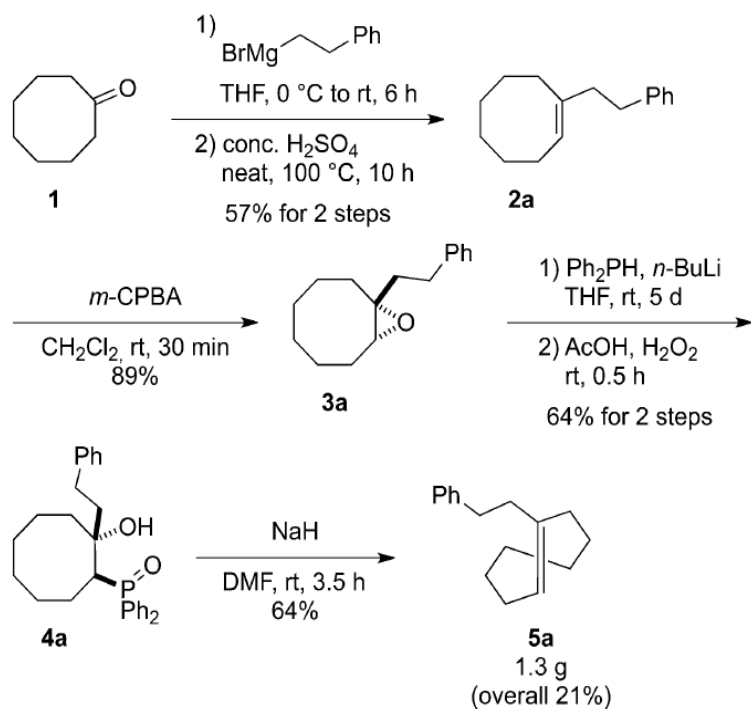
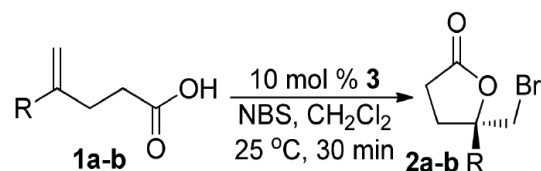
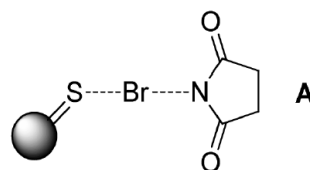
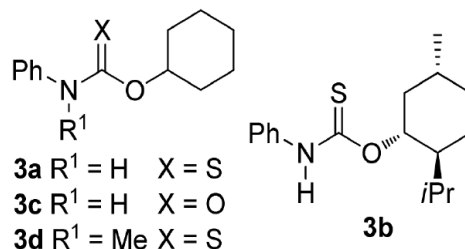


Figure 2. Synthesis and ORTEP drawing of platinum complex 6a.

Yeung Bromolactonization¹⁾



entry	catalyst	acid	R	yield ^a (%)
1	3a	1a	H	84
2	3a	1b	Ph	91
3	3b	1b	Ph	92
4 ^b	3b	1b	Ph	95
5 ^{b,c}	3b	1b	Ph	84
6	3c	1a	H	18
7	3d	1a	H	73



^a Isolated yield. ^b Reactions were conducted at -78 °C for 5 h. ^c 10 mol % of Et_3N was added.

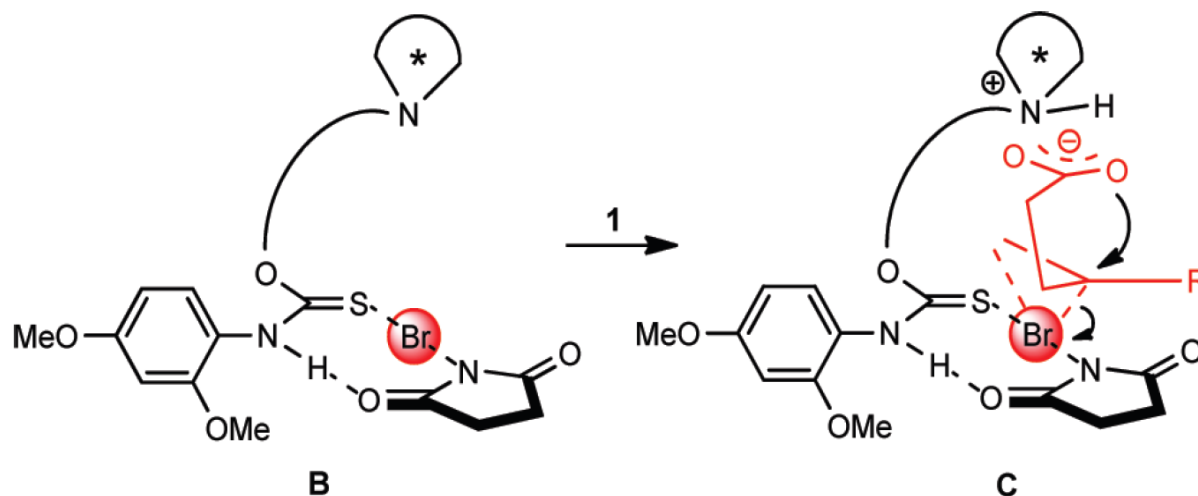
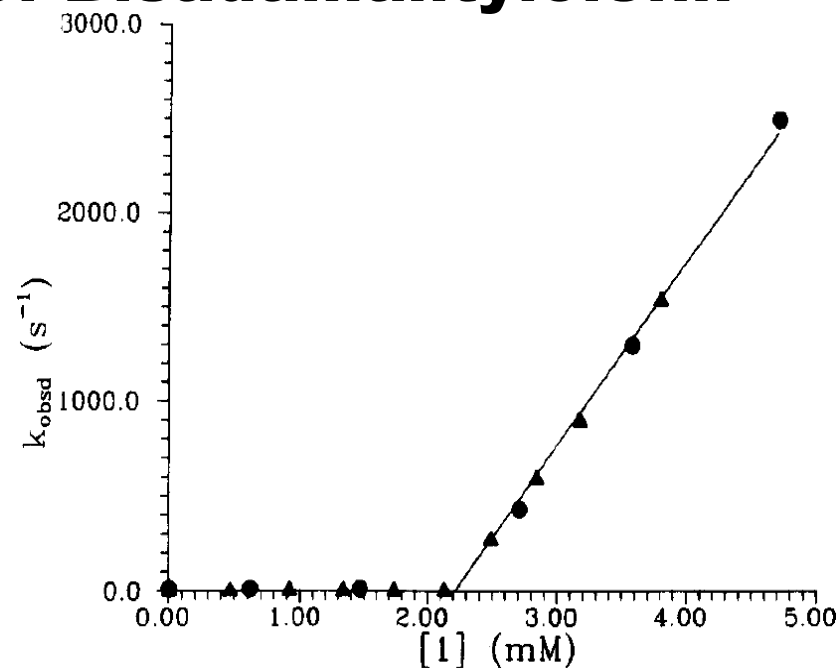
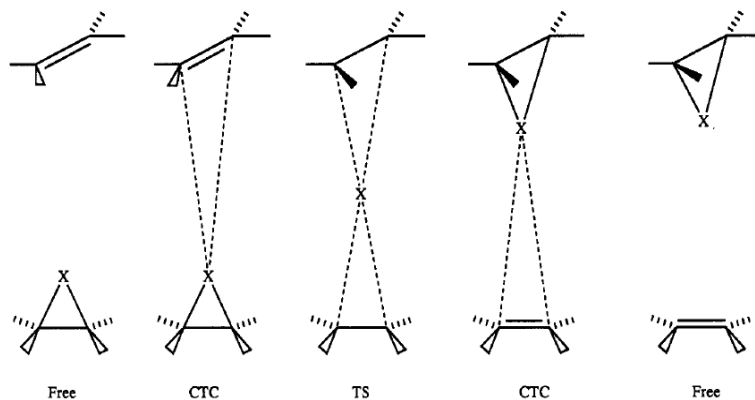
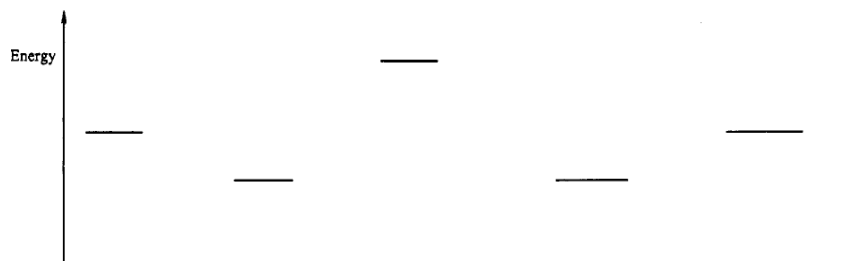
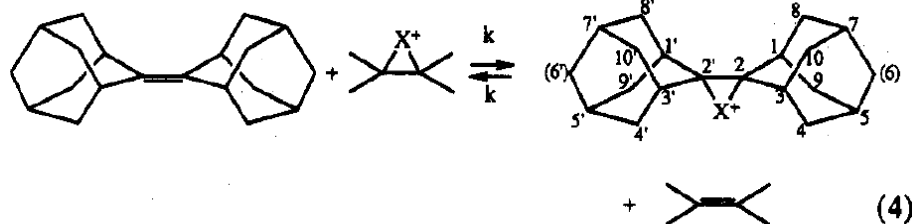
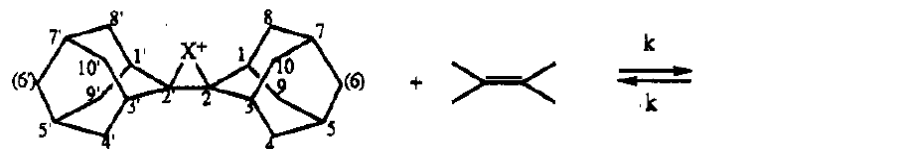


Figure 1. Proposed mechanism of the bromolactonization.

Olefin-to-olefin Transfer of Bisadamantylethenyl¹⁾



Olefin-to-olefin Transfer for Annelation¹⁾

